REMARKS

The Present Invention and the Pending Claims

The present invention relates to a method of carrying out the size separation in a sample comprising a sieving medium in a receptacle for such medium comprising a non-ionic monomeric surfactant of the general formula, B-A, wherein A is a hydrophilic moiety and B is a hydrophobic moiety, present in a solvent at a concentration forming a self-assembled micelle configuration. Related systems and methods of detecting a target also are claimed. Claims 1-32 are currently pending.

The Amendments to the Claims

Claims 1, 13, 21, and 26 have been amended to make the claims more clear. Claim 13 has been amended to add the term "at least one," which is supported by the specification at, for example, page 14, lines 10-18. Claims 9 and 17 have been amended to state the chemical names for the compounds recited therein. Accordingly, no new matter has been added by way of these amendments.

The Office Action

The Office Action made the following rejections:

(a)   claims 1-32 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite,

(b)   claims 1-5, 7, 10, 12-14, and 18 are rejected under 35 U.S.C. § 102 (b), as allegedly anticipated by or, in the alternative, under 35 U.S.C. § 103(a), as allegedly being obvious over Magnusdottir et al. (*Electrophoresis*, 19: 1699-1703 (1998)) with or without the disclosure of Rill et al. (*J. Chromatography A*, 817: 287-295 (1998)),

(c)   claims 6, 21-23, and 26-28 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the combined disclosures of Magnusdottir et al. and Liu et al. (*ACS Symposium Series*, 765: 2-20 (2000),

(d)   claims 8, 15, and 16 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the combined disclosures of Magnusdottir et al. and Menchen (U.S. Patent No. 5,290,418),

(e)   claims 31 and 32 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Magnusdottir et al. in view of Liu et al. and Menchen,

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(f)   claims 11, 15, 19, and 20 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over the combined disclosures of Magnusdottir et al. and Yeung et al. (U.S. Patent No. 5,582,705), and

(g)   claims 24, 25, and 29-31 are rejected under 35 U.S.C. § 103(a), as allegedly being unpatentable over Magnusdottir et al. in view of Liu et al. and Yeung et al.

Claims 9 and 17 would be allowable if rewritten to overcome the indefiniteness rejections and to include all of the limitations of the base claims and any intervening claims. Reconsideration of these rejections is hereby requested.

Discussion of Rejections Under 35 U.S.C. § 112, Second Paragraph

According to the Office Action, the use of the term "monomeric" with respect to the surfactant is confusing since the surfactant can be, for example, n-alkyl polyoxyethylene ether. As stated in Surfactants and Polymers In Aqueous Solutions, 1st Ed. (Jonsson et al., John Wiley and Sons (New York): May 1998, pages 1-31, copy enclosed), the term "poly" in polyoxyethylene is a misnomer (see page 14, first paragraph). Since the number of oxyethylene units is typically 5 to 10, this type of surfactant is not considered a polymer at all, and thus, is considered monomeric. Thus, use of the term "monomeric" in this instance should be considered definite.

Claims 9 and 17 are allegedly indefinite for reciting the terms $C_{14}E_6$, $C_{16}E_6$, and $C_{16}E_8$. Without a change in claim scope, these terms have been replaced with the chemical names: hexaethylene glycol monotetradecyl ether, hexaethylene glycol monohexadecyl ether, and octaethylene glycol monohexadecyl ether, respectively.

In view of the foregoing, it is submitted that the indefiniteness rejections have been overcome.

Discussion of Rejection Under 35 U.S.C. § 102(b)

Claims 1-5, 7, 10, 12-14, and 18 stand rejected under Section 102 as allegedly being anticipated in view of Magnusdottir et al. According to the Office Action, Magnusdottir et al. discloses a method of carrying out size separation according to the method of claims 1 and 13, by using a polymer of the formula B-A-B as the sieving medium. While the Office Action acknowledges that the formula B-A-B differs from the formula B-A of the pending claims, the Office Action contends that the claims use the open-ended term "comprising,"

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such that "there is nothing in the claims that prevents the groups from being connected to the B-A unit" and thus, the formula B-A-B is encompassed by the claims of the present invention. This rejection is respectfully traversed.

Pending independent claims 1, 13, 21, and 26, and thus all of the pending claims, define the sieving medium as comprising "a non-ionic monomeric surfactant of the general formula B-A." The term comprising leaves open-ended the composition of the sieving medium, but the claim makes it clear that the monomeric surfactant is of the formula "B-A." Thus, the sieving medium must have a monomeric surfactant of the formula B-A, although it may have other components, including a polymer of the formula B-A-B. The claims do not, however, read on a medium which has only a "polymeric" surfactant of the formula B-A-B. Thus, it is submitted that the rejection under 35 U.S.C. § 102(b) should be withdrawn.

Discussion of Rejections Under 35 U.S.C. § 103(a)

In addition, claims 1-8, 10-16, and 18-32 stand rejected under Section 103 as allegedly being obvious over Magnusdottir et al. either alone or in view of Rill et al., Liu et al., Menchen, and/or Yeung et al. This rejection is respectfully traversed.

Each obviousness rejection relies on Magnusdottir et al. as the primary reference. The Office relies on Rill et al.'s alleged disclosure of triblock polymers acting as surfactants and Liu et al.'s alleged disclosure of using temperature to control micelle aggregation. The Office further relies on Menchen's alleged disclosure of adding a denaturant to a sieving matrix and Yeung et al.'s alleged disclosure of using multiple capillaries for simultaneous analysis.

As discussed above, Magnusdottir et al. does not teach or suggest a non-ionic *monomeric* surfactant of the general formula, B-A. Rather, Magnusdottir et al. teaches the use of the triblock copolymer *n*-dodecane-poly(ethylene oxide)-*n*-dodecane (see abstract). The Office Action recognizes that Magnusdottir et al. teaches the use of a triblock copolymer (see Office Action, page 3, item (7)). The remaining references, namely Rill et al., Liu et al., Menchen, and Yeung et al., also do not teach or suggest a non-ionic monomeric surfactant of the general formula, B-A.

The pending claims require the use of a monomeric, i.e., a non-polymeric, non-ionic surfactant. The benefit of using non-ionic monomeric surfactants in size separation is

substantial (see specification at, for example, page 4, lines 3-19). Monomeric non-ionic surfactants are soluble in water or other suitable slightly polar organic solvents, thus low viscosity solutions can be prepared for filling the sieving medium receptacle, and then heated to an elevated temperature to provide the desired micelle configuration for effecting the size separation. The receptacle can be cleaned by dilution with the solvent after use, as disassembly of the micelle occurs. Accordingly, when a non-ionic monomeric surfactant of the general formula, B-A is used, the sieving medium is a readily handleable, low viscosity solution, except during size separation.

Moreover, the sieving media of the present invention can be readily altered as desired to tailor the medium for optimal size separation of the molecules in the specific sample involved. More specifically, the equilibrium solution of the self-assembled surfactant micelles, resulting from the use of the monomeric non-ionic surfactants, results in long rod-like micelles that can be tailored to the specific application by adjusting the surfactant concentration in the water or other solvent of use, the separation temperature and buffer additions or denaturants, so as to provide the optimal sieve medium.

The foregoing benefits cannot be found with the type of triblock copolymer used by Magnusdottir et al. and the other cited references. In contrast, a polymeric sieving medium is not always stable due to degradation with time, the testing environment and mechanical shearing during preparation. In addition, a polymeric sieving medium most commonly used is relatively difficult to use and cannot be altered since the molecular weight of the polymer fixes the application. See specification at, for example, page 2, lines 9-23.
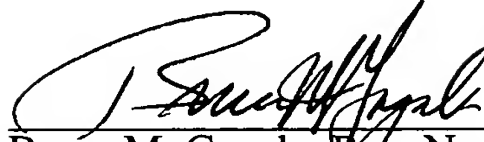
Therefore, none of the cited references, alone or in combination, teach or suggest every element of the pending claims. As such, the pending claims are novel and unobvious in view of the cited references, and the obviousness rejections should be withdrawn.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

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In re Appln. of Yeung et al.
Application No. 10/085,656

Respectfully submitted,

Bruce M. Gagala, Reg. No. 28,844
LEYDIG, VOIT & MAYER, LTD.
Two Prudential Plaza, Suite 4900
180 North Stetson Avenue
Chicago, Illinois 60601-6780
(312) 616-5600 (telephone)
(312) 616-5700 (facsimile)

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SURFACTANTS AND POLYMERS IN AQUEOUS SOLUTION

Bo Jönsson and Björn Lindman

Chemical Centre, Lund University, P.O.B. 124, S-221 00 Lund, Sweden

and

Krister Holmberg and Bengt Kronberg

Institute for Surface Chemistry, P.O.B. 5607, S-114 87 Stockholm, Sweden

1 INTRODUCTION TO SURFACTANTS

Surfactants Adsorb at Interfaces

Surfactants is an abbreviation for surface active agent, which literally means active at a surface. In other words, a surfactant is characterized by its tendency to absorb at surfaces and interfaces. The term interface denotes a boundary between any two immiscible phases; the term surface indicates that one of the phases is gas, usually air. Altogether five different interfaces exist:

Solid–vapour   *surface*
Solid–liquid
Solid–solid
Liquid–vapour   *surface*
Liquid–liquid

The driving force for a surfactant to adsorb at an interface is to lower the free energy of that phase boundary. The interfacial free energy per unit area represents the amount of work required to expand the interface. The term interfacial tension is often used instead of interfacial free energy per unit area. Thus, the surface tension of water is equivalent to the interfacial free energy per unit area of the boundary between water and the air above it. When that boundary is covered by surfactant molecules, the surface tension (or the amount of work required to expand the interface) is reduced. The denser the surfactant packing at the interface, the larger the reduction in surface tension.

Surfactants may adsorb at all the five types of interfaces listed above. Since this book concerns surfactants in solution, the discussion will be restricted to interfaces involving a liquid phase. The liquid is usually, but not always water. Examples of the different interfaces and products in which these interfaces are important are given in Table 1.1.

In many formulated products several types of interfaces are present at the same time. Water-based paints and paper coating colours are examples of familiar but, from a colloidal point of view, very complicated systems containing both solid–liquid (dispersed pigment particles) and liquid–liquid

Table 1.1   Examples of interfaces involving a liquid phase

Interface	Type of system	Product
Solid–liquid	Suspension	Solvent-borne paint
Liquid–liquid	Emulsion	Milk, cream
Liquid–vapour	Foam	Shaving cream

(latex or other binder droplets) interfaces. In addition, foam formation is a common (but unwanted) phenomenon at the application stage. All the interfaces are stabilized by surfactants. The total interfacial area of such a system is immense: the oil–water and solid–water interfaces of one litre of paint may cover several football fields.

As mentioned above, the tendency to accumulate at interfaces is a fundamental property of a surfactant. In principle, the stronger the tendency, the better the surfactant. The degree of surfactant concentration at a boundary depends on surfactant structure and also on the nature of the two phases that meet at the interface. Therefore, there is no universally good surfactant, suitable for all uses. The choice will depend on the application. A good surfactant should have low solubility in the bulk phases. Some surfactants (and several surface active macromolecules) are only soluble at the oil–water interface. Such compounds are difficult to handle but are very efficient in reducing the interfacial tension.

There is, of course, a limit to the surface and interfacial tension lowering effect by the surfactant. In the normal case that limit is reached when micelles start to form in bulk solution. Table 1.2 illustrates what effective surfactants do in terms of lowering of surface and interfacial tensions. The values given are typical of what is attained by normal light-duty liquid detergents. With special formulations so-called ultra low interfacial tension, i.e. values in the range of 10^{-3} mN/m or below, can be obtained. An example of a system giving ultra low interfacial tension is a three-phase system comprising a microemulsion in equilibrium with excess water and oil phases. Such systems are of interest for enhanced oil recovery and are discussed in Chapter 19.

Table 1.2   Typical values of surface and interfacial tensions (mN/m)

Air–water	72–73
Air–10% aqueoust NaOH	78
Air–aqueous surfactant solution	28–30
Aliphatic hydrocarbon–water	40–50
Aromatic hydrocarbon–water	20–30
Hydrocarbon–aqueous surfactant solution	1–10

Surfactants Aggregate in Solution

As discussed above, one characteristic feature of surfactants is their tendency to adsorb at interfaces. Another fundamental property of surface active agents is that unimers in solution tend to form aggregates, so-called micelles. (The free or unassociated surfactant is referred to in the literature either as 'monomer' or 'unimer'. In this text we will use 'unimer' and the term 'monomer' will be restricted to the polymer building block.) Micelle formation, or micellization, can be viewed as an alternative mechanism to adsorption at the interfaces for removing hydrophobic groups from contact with water, thereby reducing the free energy of the system. It is an important phenomenon since surfactant molecules behave very differently when present in micelles than as free unimers in solution. Only surfactant unimers contribute to surface and interfacial tension lowering and dynamic phenomena, such as wetting and foaming, are governed by the concentration of free unimers in solution. The micelles may be seen as a reservoir for surfactant unimers. The exchange rate of a surfactant molecule between micelle and bulk solution may vary by many orders of magnitude depending on the size and structure of the surfactant.

Micelles are generated already at very low surfactant concentration in water. The concentration at which micelles start to form is called the critical micelle concentration, or CMC, and is an important characteristic of a surfactant. A CMC of 1 mM, a reasonable value for an ionic surfactant, means that the unimer concentration will never exceed this value, regardless of the amount of surfactant added to the solution. Surfactant micellization is discussed in detail in Chapter 2.

Surfactants are Amphiphilic

The name amphiphile is sometimes used synonymously with surfactant. The word is derived from the Greek word *amphi*, meaning both, and the term relates to the fact that all surfactant molecules consist of at least two parts, one which is soluble in a specific fluid (the lyophilic part) and one which is insoluble (the lyophobic part). When the fluid is water one usually talks about the hydrophilic and hydrophobic parts, respectively. The hydrophilic part is referred to as the head group and the hydrophobic part as the tail (see Figure 1.1).
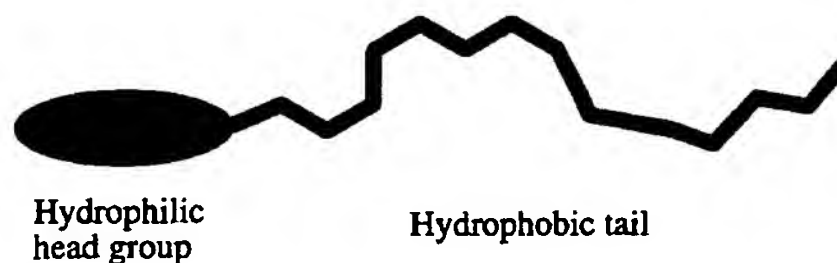

Hydrophilic
head group

Hydrophobic tail

Figure 1.1 Schematic illustration of a surfactant

In a micelle the surfactant hydrophobic group is directed towards the interior of the cluster and the polar head group is directed towards the solvent. The micelle, therefore, is a polar aggregate of high water solubility and without much surface activity. When a surfactant adsorbs from aqueous solution at a hydrophobic surface, it normally orients its hydrophobic group towards the surface and exposes its polar group to the water. The surface has become hydrophilic and, as a result, the interfacial tension between the surface and water has been reduced. Adsorption at hydrophilic surfaces often results in more complicated surfactant assemblies. Surfactant adsorption at hydrophilic and hydrophobic surfaces is discussed in Chapter 13.

The hydrophobic part of a surfactant may be branched or linear. The polar head group is usually, but not always, attached at one end of the alkyl chain. The length of the chain is in the range of 8–18 carbon atoms. The degree of chain branching, the position of the polar group and the length of the chain are parameters of importance for the physicochemical properties of the surfactant.

The polar part of the surfactant may be ionic or non-ionic and the choice of polar group determines the properties to a large extent. For non-ionic surfactants the size of the head group can be varied at will; for the ionics, the size is more or less a fixed parameter. As will be discussed many times throughout this book, the relative size of the hydrophobic and polar groups, not the absolute size of either of the two, is decisive in determining the physicochemical behaviour of a surfactant in water.

A surfactant usually contains only one polar group. Recently, there has been considerable research interest in certain dimeric surfactants, containing two hydrophobic tails and two head groups linked together with a short spacer. These species, generally known under the name gemini surfactants, are not yet of commercial importance. They show several interesting physicochemical properties, such as very high efficiency in lowering surface tension and very low CMC. The low CMC values of gemini surfactants can be illustrated by a comparison of the value for the conventional cationic surfactant dodecyltrimethylammonium bromide (16 mM) and that of the corresponding gemini surfactant, having a 2 carbon linkage between the monomers (0.9 mM). The difference in CMC between monomeric and dimeric surfactants could be of considerable practical importance. A typical gemini surfactant is shown in Figure 1.2.

Weakly surface active compounds which accumulate at interfaces but which do not readily form micelles are of interest as additives in many surfactant formulations. They are referred to as hydrotropes and serve the purpose of destroying the ordered packing of ordinary surfactants. Thus, addition of a hydrotrope is a way to prevent the formation of highly viscous liquid crystalline phases which constitutes a well-known problem in surfactant formulations. Xylene sulfonate and cumene sulfonate are typical examples of hydrotropes used, for instance, in detergent formulations. Short-chain alkyl phosphates have found specific use as hydrotropes for longer-chain alcohol ethoxylates.
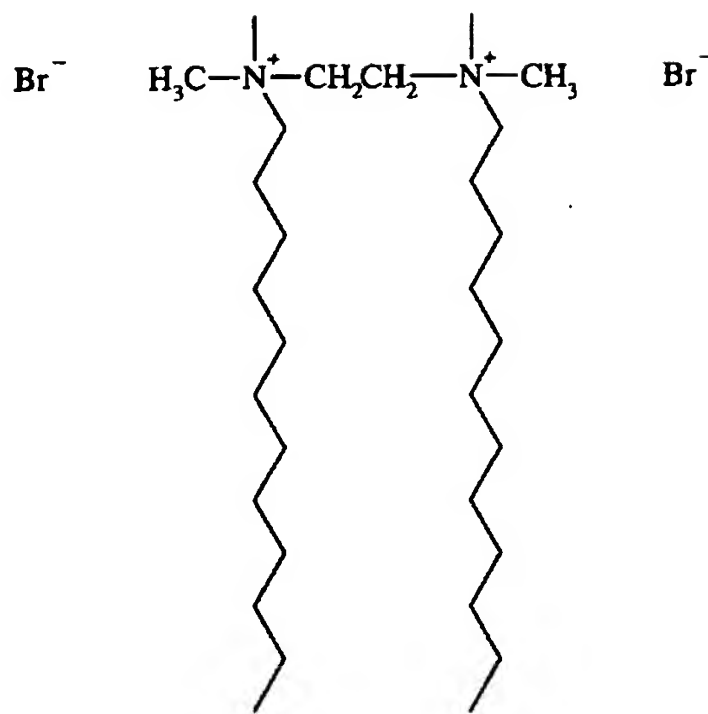
$$Br^- \quad H_3C-\overset{|}{\underset{|}{N^+}}-CH_2CH_2-\overset{|}{\underset{|}{N^+}}-CH_3 \quad Br^-$$

Figure 1.2 A gemini surfactant

Surface Active Compounds are Plentiful in Nature

Nature's own surfactants are usually referred to as polar lipids. These are abundant in all living organisms. In biological systems the surface active agents are used in very much the same way as surfactants are employed in technical systems: to overcome solubility problems, as emulsifiers, as dispersants, to modify surfaces, etc. Figure 1.3 gives examples of important polar lipids. The only important examples of surfactant being obtained directly, without chemical conversion, from nature is lecithin. (The term lecithin is not used in a strict way in the surfactant literature. It is sometimes used synonymously with phosphatidylcholine and it sometimes refers to phospholipids in general). Lecithin is extracted from phospholipid-rich sources such as soybean and egg.

Micro-organisms are sometimes efficient producers of surface active agents. Both high molecular weight compounds, e.g. lipopolysaccharides, and low molecular weight polar lipids can be produced in good yields, particularly when the micro-organism is fermented on a water-insoluble substrate. Surface active polymers of this type are dealt with in Chapter 10. Figure 1.4 gives the structure of a low molecular weight acylated sugar, a trehalose lipid, which has proved to be an effective surfactant. Trehalose lipids and several other surface active agents produced from bacteria and yeasts have attracted considerable interest in later years and much effort has been directed towards improving the fermentation and, not least, the work-up procedure. Although considerable process improvements have been made, commercial use of these products is still very limited due to their high price.

Surfactant Raw Materials May Be Based on Petrochemicals or Oleochemicals

For several years there has been a strong trend towards 'green' surfactants, particularly for the household sector. In this context the term 'natural surfactant' is often used to indicate some natural origin or the compound. However, no surfactants used in any substantial quantities today are truly natural. With few exceptions they are all manufactured by organic synthesis, usually involving rather hard conditions
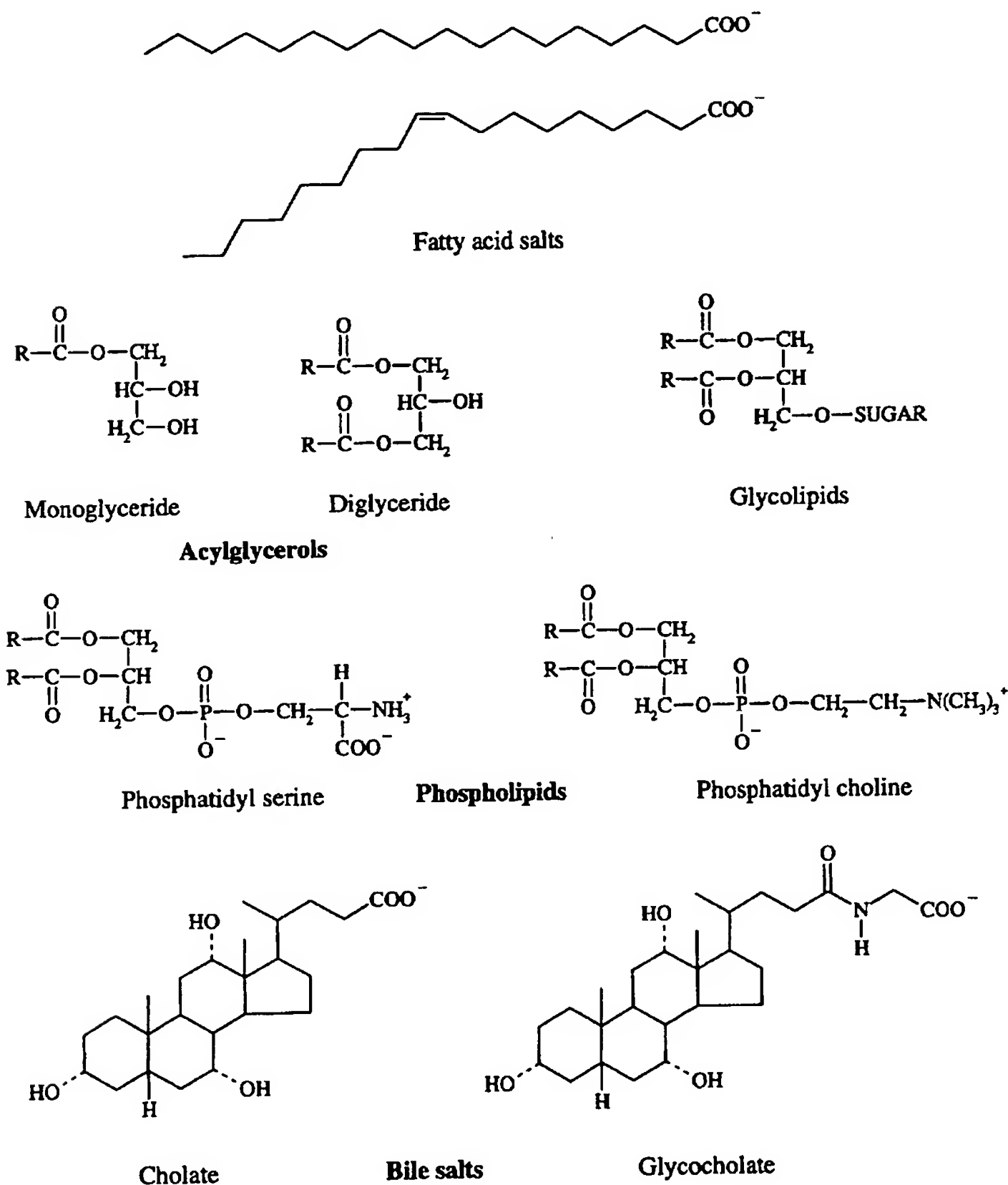

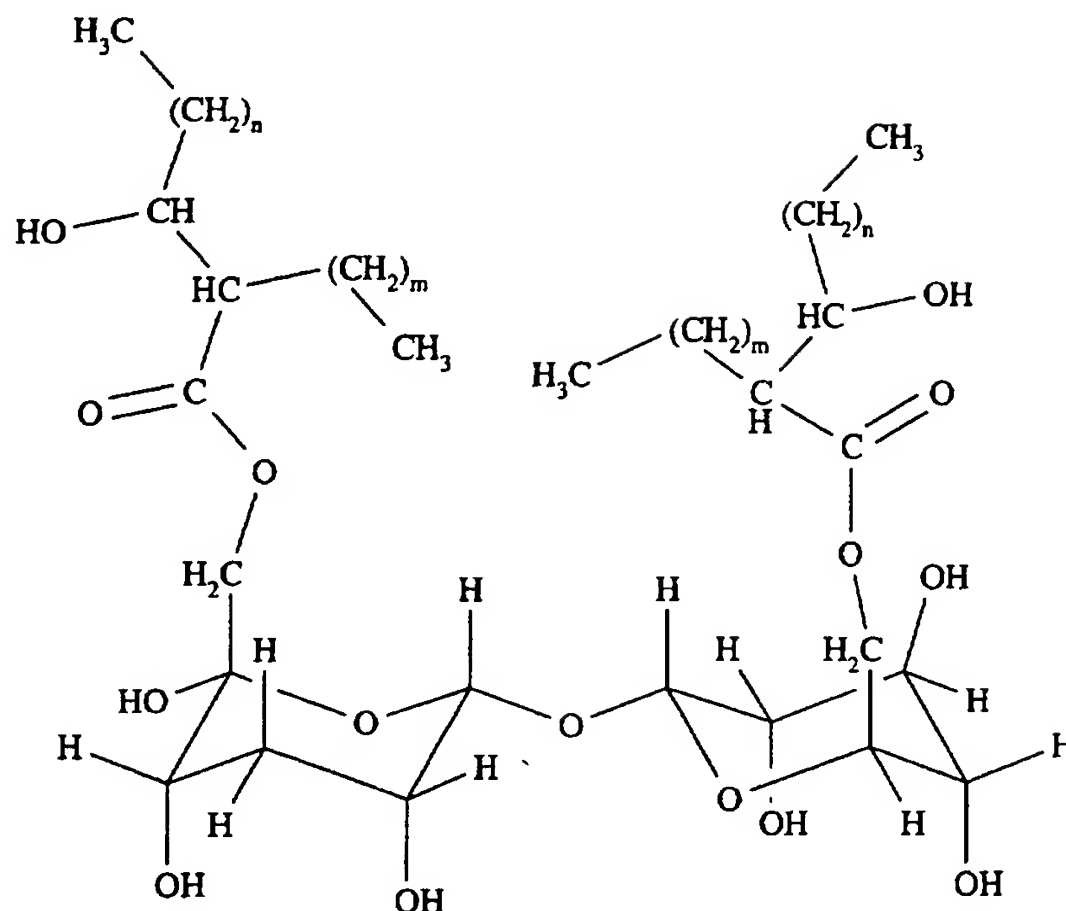Figure 1.3 Examples of polar lipids

Figure 1.4 A surface active trehalose lipid produced by fermentation

which inevitably give by-products. For instance, monoglycerides are certainly available in nature, but the surfactants sold as monoglycerides are prepared by glycerolysis of triglyceride oils at temperatures well above 200°C, yielding di- and triglycerol derivatives as by-products. Alkyl glucosides are abundant in living organisms but the surfactants of this class, often referred to as APGs (alkyl polyglucosides), are made in several steps which by no means are natural.

A more adequate approach to the issue of origin is to divide surfactants into oleochemically based and petrochemically based surfactants. Surfactants based on oleochemicals are made from renewable raw materials, most commonly vegetable oils. Surfactants from petrochemicals are made from small building blocks, such as ethylene, produced by cracking of nafta. Quite commonly, a surfactant may be built up by raw materials from both origins. Fatty acid ethoxylates are one example out of many.

Sometimes the oleochemical and the petrochemical pathways lead to essentially identical products. For instance, linear alcohols in the C10–C14 range, which are commonly used as hydrophobes for both non-ionics (alcohol ethoxylates) and anionics (alkyl sulfates, alkyl phosphates, etc.), are made either by hydrogenation of the corresponding fatty acid methyl esters or via Ziegler–Natta polymerization of ethylene using triethyl aluminium as catalyst. Both routes yield straight-chain alcohols and the homologue distribution is not very different since it is largely governed by the distillation process. Both pathways are used in very large scale operations.

It is not obvious that the oleochemical route will lead to a less toxic and more environmentally friendly surfactant than the petrochemical route. However, from the carbon dioxide cycle point of view chemical production based on renewable raw materials is always preferred.

Linear long-chain alcohols are often referred to as fatty alcohols, regardless of their source. Branched alcohols are also of importance as surfactant raw material. They are invariably produced by synthetic routes, the most common being the so-called oxo process, in which an olefin is reacted with carbon monoxide and hydrogen to give an aldehyde, which is subsequently reduced to the alcohol by catalytic hydrogenation. A mixture of branched and linear alcohols is obtained and the ratio between the two can be varied to some extent by the choice of catalyst and reaction conditions. The commercial 'oxo alcohols' are mixtures of linear and branched alcohols of specific alkyl chain length ranges. The different routes to higher molecular weight primary alcohols are illustrated in Figure 1.5.

Surfactants are Classified by the Polar Head Group

The primary classification of surfactants is made on the basis of the charge of the polar head group. It is common practice to divide surfactants into the classes anionics, cationics, non-ionics and zwitterionics. Surfactants belonging to the latter class contain both an anionic and a cationic charge under normal conditions. In the literature they are often referred to as amphoteric surfactants but the term 'amphoteric' is not always correct and should not be used as synonymous to zwitterionics. An amphoteric surfactant is one that, depending on pH, can be either cationic, zwitterionic or anionic. Among normal organic substances, simple amino acids are well-known examples of amphoteric compounds. Many so-called zwitterionic surfactants are of this category. However, other zwitterionic surfactants retain one of the charges over the whole pH range. Compounds with a quaternary ammonium as the cationic group are examples of that. Consequently, a surfactant that contains a carboxylate group and a quarternary ammonium group, a not uncommon combination as we shall see later in this Chapter, is zwitterionic unless the pH is very low, but is not an amphoteric surfactant.

Most ionic surfactants are monovalent but there are also important examples of divalent anionic amphiphiles. For the ionic surfactants the choice of counterion plays a role for the physicochemical properties. Most anionic surfactants have sodium as counterion but other cations, such as lithium, potassium, calcium and protonated amines, are used as surfactant counterions for speciality purposes. The counterion of cationic surfactants is usually a halide or methyl sulfate.

The hydrophobic group is normally hydrocarbon (alkyl or alkylaryl) but may also be polydimethylsiloxane or fluorocarbon. The two latter types of surfactants are particularly effective in non-aqueous systems.
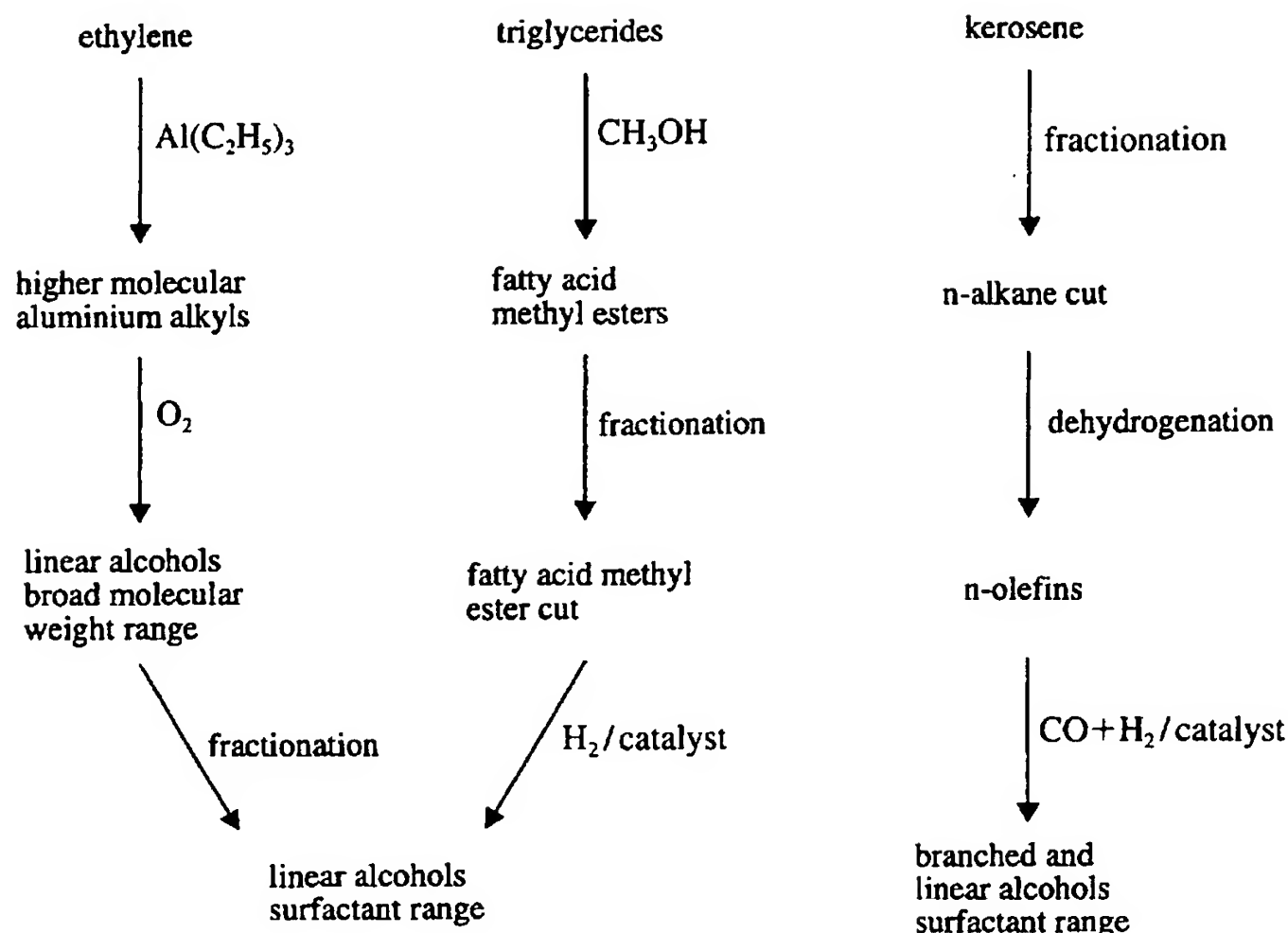
ethylene

$Al(C_2H_5)_3$

higher molecular
aluminium alkyls

O_2

linear alcohols
broad molecular
weight range

fractionation

linear alcohols
surfactant range

triglycerides

CH_3OH

fatty acid
methyl esters

fractionation

fatty acid methyl
ester cut

H_2/catalyst

kerosene

fractionation

n-alkane cut

dehydrogenation

n-olefins

$CO+H_2$/catalyst

branched and
linear alcohols
surfactant range

Figure 1.5 Different pathways for preparation of primary alcohols of interest as surfactant raw materials. From left to right: Ziegler–Natta polymerization of ethylene, reduction of fatty acid methyl esters, hydroformylation of higher olefins (the oxo process)

For a few surfactants there is some ambiguity as to classification. For example, amine oxide surfactants are sometimes referred to as zwitterionics, sometimes as cationics and sometimes as non-ionics. Their charge is pH dependent and in the net neutral state they may either be seen as having distinct anionic and cationic charges or as dipolar non-ionic compounds. Fatty amine ethoxylates which contain both an amino nitrogen atom (cationic polar group) and a polyoxyethylene chain (non-ionic polar group) may be included in either the cationics or the non-ionics class. The non-ionic character dominates when the polyoxyethylene chain is very long, whereas for medium and short chains the physicochemical properties are mainly those of cationic surfactants. Surfactants containing both an anionic group, such as sulfate, phosphate or carboxylate, and a polyoxyethylene chain are also common. These surfactants, known as ether sulfates etc., invariably contain short polyoxyethylene chains, typically two or three oxyethylene units, and are therefore always categorized as anionics.

Anionics

Carboxylate, sulfate, sulfonate and phosphate are the polar groups found in anionic
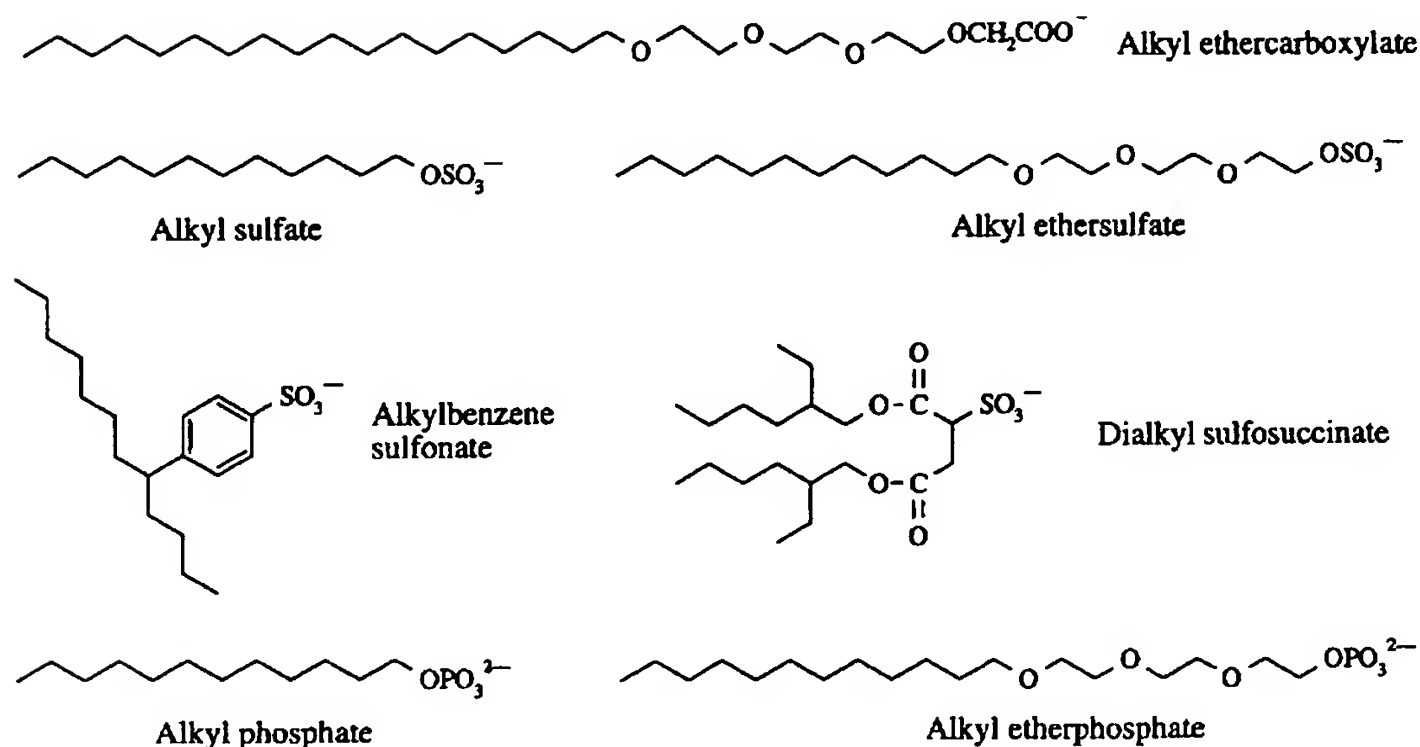
Figure 1.6 Structures of representative anionic surfactants

surfactants. Figure 1.6 shows structures of the more common surfactant types belonging to this class.

Anionics are used in greater volume than any other surfactant class. One main reason for their popularity is the ease and low cost of manufacture. Anionics are used in most detergent formulations and best detergency is obtained by paraffin chains in the C12–C16 range.

The counterions most commonly used are sodium, potassium, ammonium, calcium and various protonated alkyl amines. Sodium and potassium impart water solubility, whereas calcium and magnesium promote oil solubility. Amine/alkanol amine salts give products with both oil and water solubility.

Soap is still the largest single type of surfactant. It is produced by saponification of natural oils and fats. Soap is a generic name representing the alkali metal salt of a carboxylic acid derived from animal fats or vegetable oils. Soap bars are usually based on mixtures of fatty acids obtained from tallow, coconut and palm oil. Under the right conditions soaps are excellent surfactants. Their sensitivity to hard water is a major drawback, however, and has constituted a major driving force for the development of synthetic surfactants.

Alkylbenzene sulfonates have traditionally been the work-horse among synthetic surfactants. They are widely used in household detergents as well as in a variety of industrial applications. They are made by sulfonation of alkylbenzenes. In large-scale synthesis sulfur trioxide is the sulfonating agent of choice but other reagents, such as sulfuric acid, oleum ($H_2SO_4 nSO_3$), chlorosulfonic acid ($ClSO_3H$) or amidosulfonic acid (sulfamic acid, H_2NSO_3H), may also be used and may be preferred for specific purposes. Industrial synthesis is usually made in a continuous process, using a falling film reactor. The first step of the synthesis results in the
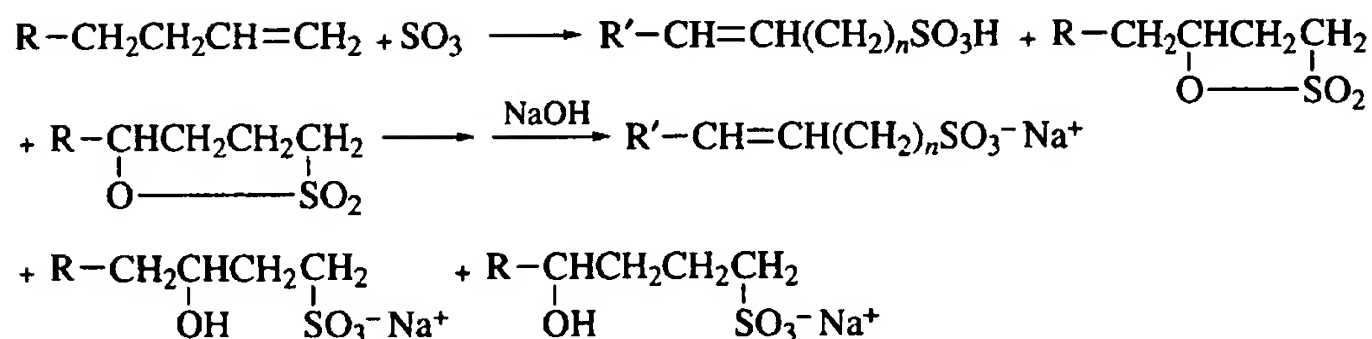
formation of pyrosulfonic acid which slowly and spontaneously reacts further to give the sulfonic acid.
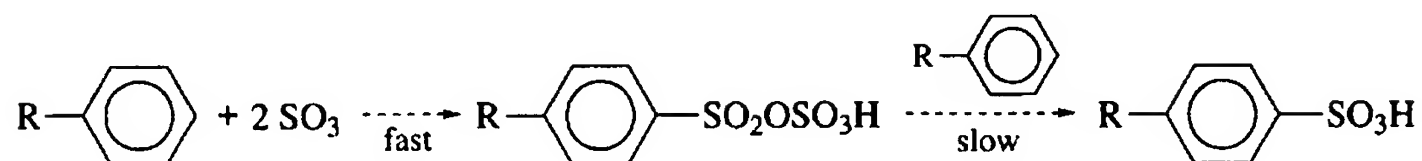
The sulfonic acid is subsequently neutralized, usually by caustic soda, to give the surface active alkylbenzene sulfonate salt. Due to the bulkiness of the alkyl substituent, the process gives almost exclusively *p*-sulfonation. R in the scheme above is typically an alkyl group of 12 carbon atoms. Originally, alkylbenzenes as surfactant intermediates were based on branched alkyls, but these have now almost entirely been replaced by their linear counterparts, thus giving the name linear alkylbenzene sulfonate (LABS or LAS). Faster biodegradation has been the main driving force for the transition to chains without branching. Alkylbenzenes are made by alkylation of benzene with an n-alkene or with alkyl chloride using HF or $AlCl_3$ as catalyst. The reaction yields a mixture of isomers with the phenyl group attached to one of the non-terminal positions of the alkyl chain.

Other sulfonate surfactants that have found use in detergent formulations are paraffin sulfonates and α-olefin sulfonates, the latter often referred to as AOS. Both are complex mixtures of compounds with varying physicochemical properties. Paraffin sulfonates, or secondary n-alkane sulfonates, are mainly produced in Europe. They are usually prepared by sulfoxidation of paraffin hydrocarbons with sulfur dioxide and oxygen under UV (ultraviolet) irradiation. In an older process, which is still in use, paraffin sulfonates are made by sulfochlorination. Both processes are free radical reactions and since secondary carbons give much more stable radicals than primary, the sulfonate group will be introduced more or less randomly on all non-terminal carbon atoms along the alkane chain. A C_{14}–C_{17} hydrocarbon cut, sometimes called the Euro cut, is normally used as hydrophobe raw material. Thus, the product obtained will be a very complex mixture of both isomers and homologues.

α-Olefin sulfonates are prepared by reacting linear α-olefins with sulfur trioxide, typically yielding a mixture of alkene sulfonate (60–70%), 3- and 4-hydroxyalkane sulfonates (around 30%) and some disulfonate and other species. The two main α-olefin fractions used as starting material are C_{12}–C_{16} and C_{16}–C_{18}. The ratio of alkene sulfonate to hydroxyalkane sulfonate is to some degree governed by the ratio of SO_3 to olefin: the higher the ratio the more alkene sulfonic acid will be formed. Formation of hydroxyalkane sulfonic acid proceeds via a cyclic sultone, which is subsequently cleaved by alkali. The sultone is toxic and it is important that its concentration in the end-product is very low. The route of preparation can be written:

$$R-CH_2CH_2CH=CH_2 + SO_3 \longrightarrow R'-CH=CH(CH_2)_nSO_3H + R-CH_2\underset{\underset{SO_2}{|}}{\overset{\overset{}{|}}{C}}HCH_2CH_2$$

$$+ R-\underset{\underset{SO_2}{|}}{\overset{\overset{}{|}}{C}}HCH_2CH_2CH_2 \xrightarrow{\quad NaOH \quad} R'-CH=CH(CH_2)_nSO_3^- Na^+$$

$$+ R-CH_2\underset{\underset{OH}{|}}{C}H\underset{\underset{SO_3^- Na^+}{|}}{C}H_2CH_2 \quad + R-\underset{\underset{OH}{|}}{C}HCH_2CH_2\underset{\underset{SO_3^- Na^+}{|}}{C}H_2$$

An alkyl sulfonate surfactant widely used in surface chemistry research is sodium di(2-ethylhexyl)sulfosuccinate, often referred to by its American Cyanamid trade name Aerosol OT, or AOT. AOT, with its bulky hydrophobe structure (see Figure 1.6), is particularly useful for preparation of w/o (water/oil) microemulsions, as is discussed in Chapter 18.

Isethionate surfactants, with the general formula R—COOCH$_2$CH$_2$SO$_3^-$Na$^+$, are fatty acid esters of isethionic acid salt. They are among the mildest sulfonate surfactants and are used in cosmetics formulations.

Very crude sulfonate surfactants are obtained by sulfonation of lignin, petroleum fractions, alkylnaphthalenes or other low-cost hydrocarbon fractions. Such surfactants are used in a variety of industrial applications as dispersants, emulsifiers, demulsifiers, defoamers, wetting agents, etc.

Sulfated alcohols and alcohol ethoxylates constitute another important group of anionics, widely used in detergent formulations. They are monoesters of sulfuric acid and the ester bond is a labile linkage which splits with particular ease at low pH where hydrolysis is autocatalytic. Both linear or branched alcohols, typically with eight to sixteen carbon atoms, are used as raw materials. The linear twelve-carbon alcohol leads to dodecylmonoester of sulfuric acid and, after neutralization with caustic soda, to sodium dodecyl sulfate (SDS), which is by far the most important surfactant within this category. The alcohol ethoxylates used as intermediates are usually fatty alcohols with two or three oxyethylene units. The process is similar to the sulfonation discussed above. Sulfur trioxide is the reagent used for large-scale production and, in analogy to sulfonation, the reaction proceeds via an intermediate pyrosulfate:

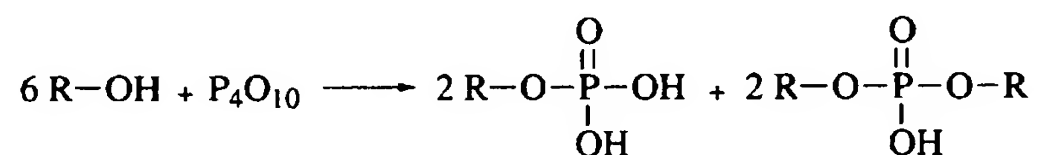$$R-OH + 2SO_3 \xrightarrow[fast]{} R-O-SO_2OSO_3H \xrightarrow[slow]{R-OH} R-O-SO_3H$$
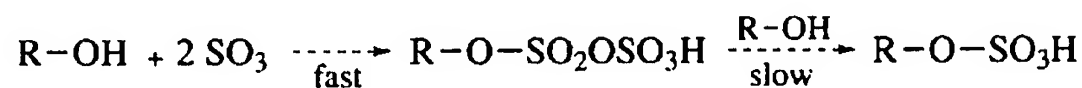
Synthesis of sulfate esters of ethoxylated alcohols proceeds similarly. In this reaction 1,4-dioxane is usually formed in non-negligible amounts. Since dioxane is toxic, its removal by evaporation is essential. These surfactants are usually referred to as ether sulfates. Ether sulfates are good at producing foams and have a low toxicity to the skin and eye. They are popular in hand dishwashing and shampoo formulations.

Ethoxylated alcohols may also be transformed into carboxylates to give ether carboxylates. These have traditionally been made from sodium monochloroacetate using the Williamson ether synthesis:

$$R-(OCH_2CH_2)_n-OH + ClCH_2COO^-Na^+ \longrightarrow$$

$$R-(OCH_2CH_2)_n-O-CH_2COOH + NaCl$$
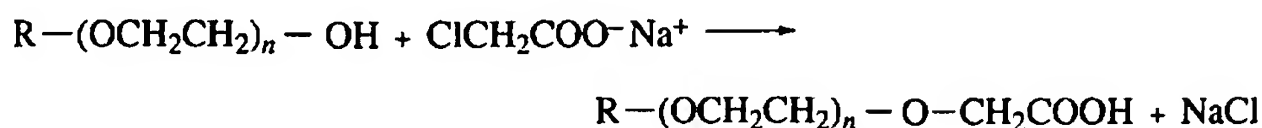
The Williamson synthesis usually does not proceed quantitatively. A more recent synthetic procedure involves oxygen or peroxide oxidation of the alcohol ethoxylate in alkaline solution using palladium or platinum catalyst. This reaction gives conversion of the ethoxylate in very high yield, but may also lead to oxidative degradation of the polyoxyethylene chain. Ether carboxylates have found use in personal care products and are also used as a cosurfactant in various liquid detergent formulations. Like ether sulfates, ether carboxylates are very tolerant to high water hardness. Both surfactant types also exhibit good lime soap dispersing power, which is an important property for a surfactant in personal care formulations. Lime soap dispersing power is usually defined as the number of grams of surfactant required to disperse the lime soap formed from 100 g of sodium oleate in water with a hardness equivalent of 333 ppm of $CaCO_3$.

Phosphate-containing anionic surfactants, both alkyl phosphates and alkyl ether phosphates, are made by treating the fatty alcohol or alcohol ethoxylate with a phosphorylating agent, usually phosphorus pentoxide, P_4O_{10}. The reaction yields a mixture of mono- and diesters of phosphoric acid, and the ratio between the esters is governed by the ratio of the reactants and the amount of water in the reaction mixture:

$$6\,R-OH + P_4O_{10} \longrightarrow 2\,R-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}}-OH + 2\,R-O-\overset{\overset{\displaystyle O}{\|}}{\underset{\underset{\displaystyle OH}{|}}{P}}-O-R$$

All commercial phosphate surfactants contain both mono- and diesters of phosphoric acid, but the relative amounts vary from one producer to another. Since the physico-chemical properties of the alkyl phosphate surfactants depend on the ratio of the esters, alkyl phosphates from different suppliers are less interchangeable than other surfactants. Phosphorus oxychloride, $POCl_3$, can also be used as a phosphorylating agent to produce alkyl phosphate surfactants. Also with $POCl_3$ a mixture of mono- and diesters of phosphoric acid is obtained.

Phosphate surfactants are used in the metal working industry where advantage is taken of their anticorrosive properties. They are also used as emulsifiers in plant protection formulations. Important facts about anionic surfactants are given in Table 1.3.

Table 1.3 Important facts about anionic surfactants

---

1. They are by far the largest surfactant class.
2. They are generally not compatible with cationics (although there are important exceptions).
3. They are generally sensitive to hard water. Sensitivity decreases in the order carboxylate > phosphate > sulfate ≃ sulfonate.
4. A short polyoxyethylene chain between the anionic group and the hydrocarbon improves salt tolerance considerably.
5. A short polyoxypropylene chain between the anionic group and the hydrocarbon improves solubility in organic solvents (but may reduce the rate of biodegradation).
6. Sulfates are rapidly hydrolysed by acids in an autocatalytic process. The other types are stable unless extreme conditions are used.

Non-ionics

Non-ionic surfactants have either polyether or polyhydroxyl as the polar group. In the vast majority of non-ionics, the polar group is polyether consisting of oxyethylene units, made by polymerization of ethylene oxide. Strictly speaking, the prefix 'poly' is a misnomer. The typical number of oxyethylene units in the polar chain is five to ten, although some surfactants, e.g. dispersants, often have much longer oxyethylene chains. Ethoxylation is usually carried out under alkaline conditions. Any material containing an active hydrogen can be ethoxylated. The most commonly used starting materials are fatty alcohols, alkylphenols, fatty acids and fatty amines. Esters, e.g. triglyceride oils, may be ethoxylated in a process that involves alkaline ester hydrolysis followed by ethoxylation of the acid and alcohol formed and subsequent partial condensation of the ethoxylated species. Castor oil ethoxylates, used for animal feed applications, constitute an interesting example of triglyceride-based surfactants.

Examples of polyhydroxyl (polyol)-based surfactants are sucrose esters, sorbitan esters, alkyl glucosides and polyglycerol esters, the latter type actually being a combination of polyol and polyether surfactant. Polyol surfactants may also be ethoxylated. A common example is fatty acid esters of sorbitan (known under the Atlas trade name of Span) and the corresponding ethoxylated products (known as Tween). The five-membered ring structure of sorbitan is formed by dehydration of sorbitol during manufacture. The sorbitan ester surfactants are edible and, hence, useful for food and drug use. Acetylenic glycols, surfactants containing a centrally located acetylenic bond and hydroxyl groups at the adjacent carbon atoms, constitute a special type of hydroxyl-based surfactant, which have found use as antifoam agent, particularly in coatings applications.

Figure 1.7 gives structures of the more common non-ionic surfactants. It should be stressed that a commercial oxyethylene-based surfactant consists of a very broad spectrum of compounds, broader than for most other surfactant types. Fatty acid ethoxylates constitute particularly complex mixtures with high amounts of
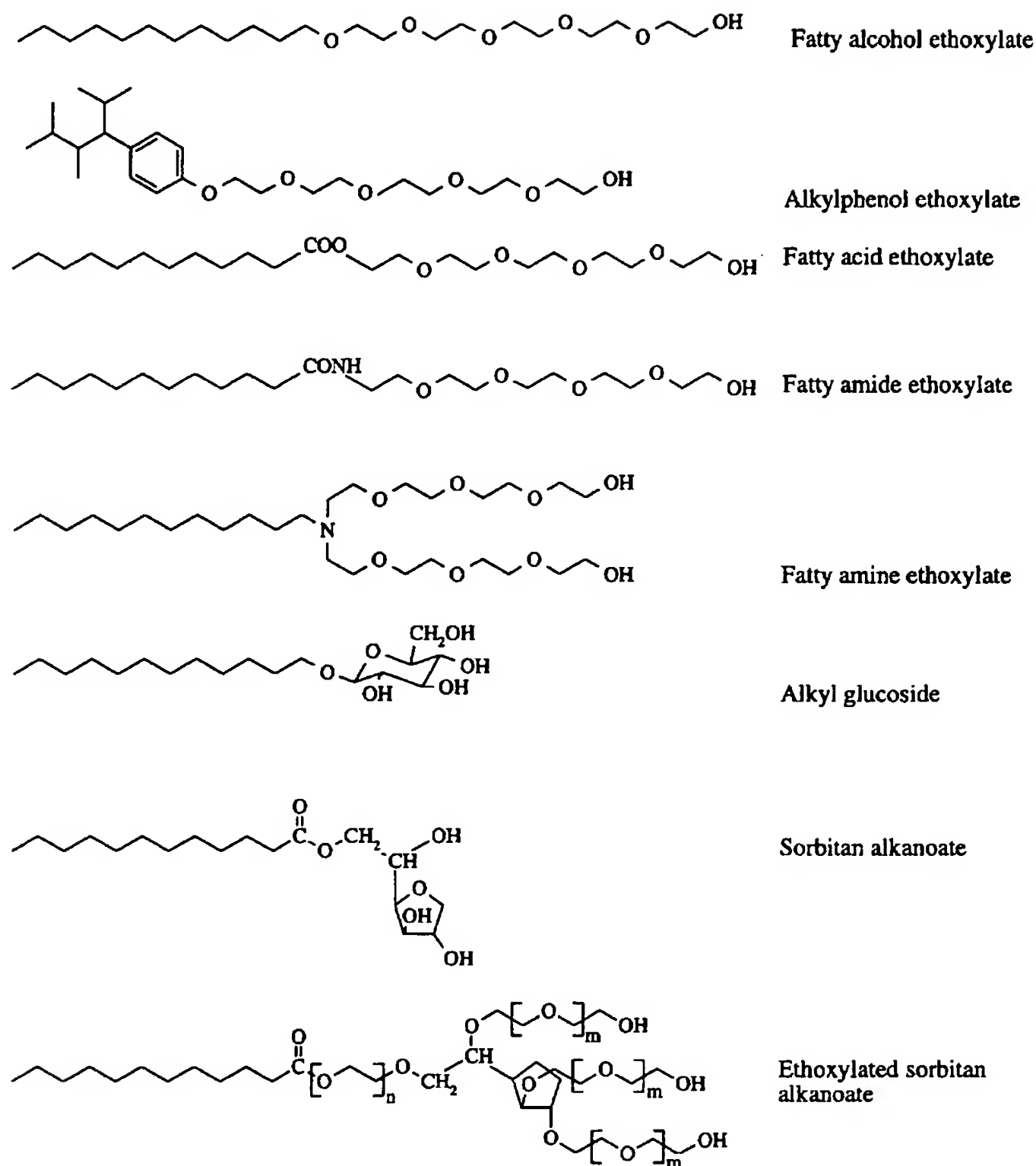
Figure 1.7 Structures of representative non-ionic surfactants

poly(ethylene glycol) and fatty acid as by-products. The single most important type of non-ionic surfactant is fatty alcohol ethoxylates. They are used in liquid and powder detergents as well as in a variety of industrial applications. They are particularly useful to stabilize oil-in-water emulsions and their use as an emulsifier is discussed in some detail in Chapter 17. Fatty alcohol ethoxylates can be regarded as hydrolytically stable in the pH range 3–11. They undergo a slow oxidation in air, however, and some oxidation products, e.g. aldehydes, are more irritating to the skin than the intact surfactant. Throughout this text fatty alcohol ethoxylates are referred to as $C_n E_m$ with n being the number of carbon atoms in the alkyl chain and
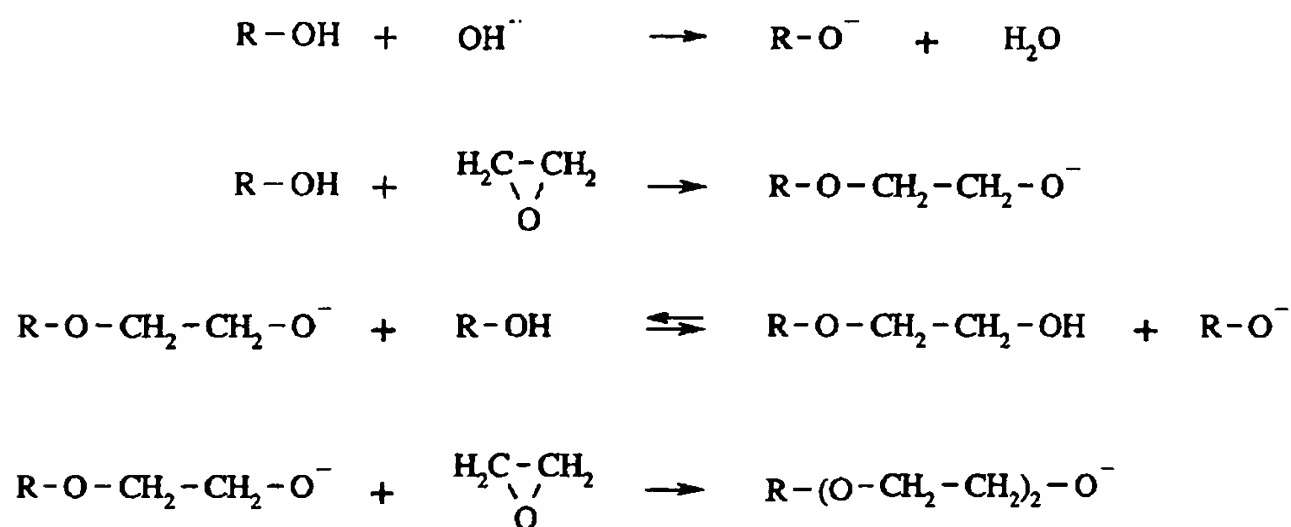
Table 1.4   Important facts about non-ionic surfactants

1. They are the second largest surfactant class.
2. They are normally compatible with all other types of surfactants.
3. They are not sensitive to hard water.
4. Contrary to ionic surfactants, their physicochemical properties are not markedly affected by electrolytes.
5. The physicochemical properties of ethoxylated compounds are very temperature dependent. Contrary to ionic compounds they become less water soluble—more hydrophobic—at higher temperatures. Sugar-based non-ionics exhibit the normal temperature dependence, i.e. their solubility in water increases with temperature.

m being the number of oxyethylene units. Important facts about non-ionic surfactants are given in Table 1.4.

Ethoxylated surfactants can be tailor-made with high precision with regard to the average number of oxyethylene units added to a specific hydrophobe, e.g. a fatty alcohol. However, the ethoxylation invariably gives a broad distribution of chain lengths. If all hydroxyl groups, i.e. those of the starting alcohol and the glycol ethers formed, had the same reactivity, a Poisson distribution of oligomers would be obtained. Since the starting alcohol is slightly less acidic than the glycol ethers, its deprotonation is disfavoured, leading to a lower probability for reaction with ethylene oxide. The reaction scheme is given in Figure 1.8.

Hence, a considerable amount of unethoxylated alcohol will remain in the reaction mixture, also with relatively long ethoxylates. This is sometimes a problem and considerable efforts have been made to obtain a more narrow homologue distribution. The distribution can be affected by the choice of ethoxylation catalyst and it has found that alkaline earth hydroxides, such as $Ba(OH)_2$ and $Sr(OH)_2$, give a much more narrow distribution than KOH, probably due to some co-ordination mechanism. Also Lewis acids, e.g. $SnCl_4$ and BF_3, give narrow distributions. Acid catalysed ethoxylation suffers from the drawback of 1,4-dioxane being formed in considerable quantities as by-product. Therefore, this process can only be used to

$$R-OH + OH^- \longrightarrow R-O^- + H_2O$$

$$R-OH + \underset{O}{\overset{H_2C-CH_2}{\diagdown\diagup}} \longrightarrow R-O-CH_2-CH_2-O^-$$

$$R-O-CH_2-CH_2-O^- + R-OH \rightleftharpoons R-O-CH_2-CH_2-OH + R-O^-$$

$$R-O-CH_2-CH_2-O^- + \underset{O}{\overset{H_2C-CH_2}{\diagdown\diagup}} \longrightarrow R-(O-CH_2-CH_2)_2-O^-$$

Figure 1.8   Base catalysed ethoxylation of a fatty alcohol, R——OH
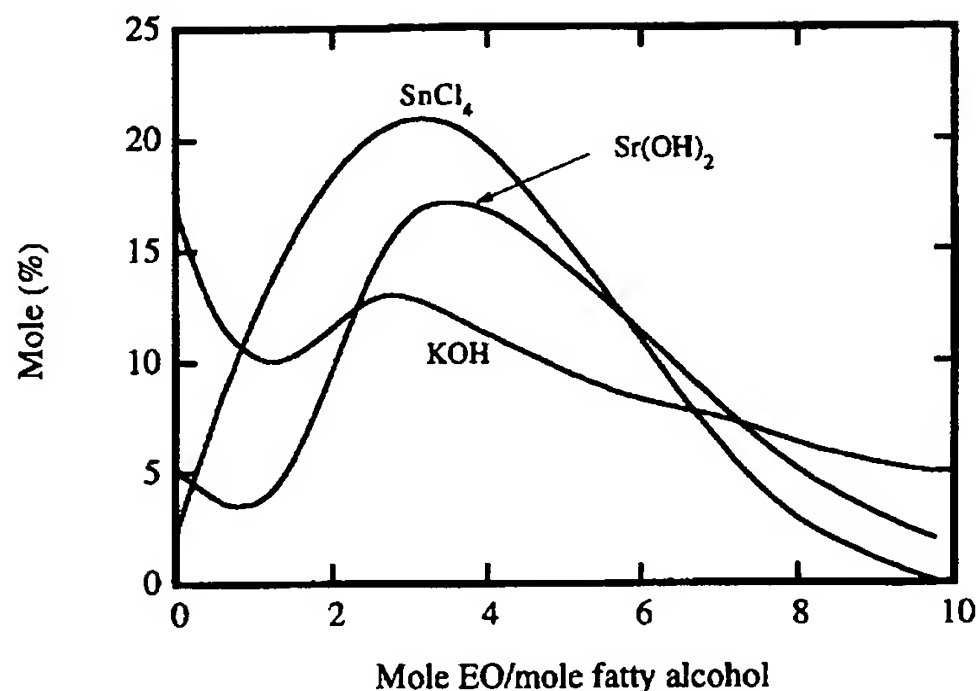
Figure 1.9 Typical homologue distributions of a fatty alcohol reacted with 4 moles of ethylene oxide (EO) using different ethoxylation catalysts

prepare short ethoxylates. In Figure 1.9 the homologue distribution of a conventional alcohol ethoxylate, using KOH as catalyst, is compared with ethoxylates prepared using a Lewis acid and an alkaline earth hydroxide as catalyst.

So-called peaked ethoxylates have a growing share of the market. Typical advantages of ethoxylates with peaked distribution are that:

(1) The low content of free alcohol reduces smell.
(2) The low content of free alcohol reduces pluming during spray-drying.
(3) The low content of low oxyethylene homologues increases solubility.
(4) The low content of high oxyethylene homologues reduces viscosity.
(5) In alkyl ether sulfates the low content of alkyl sulfate reduces skin irritation.

As mentioned in Table 1.4, non-ionic surfactants containing polyoxyethylene chains exhibit reverse solubility versus temperature behaviour in water. On raising the temperature two phases eventually appear. The temperature at which this occurs is referred to as the cloud point, alluding to the fact that the solution becomes turbid. The cloud point depends on both the hydrophobe chain length and the number of oxyethylene units, and it can be determined with great accuracy. In the manufacture of polyoxethylene-based surfactants, cloud point determination is used as a way to monitor the degree of ethoxylation. The onset of turbidity varies somewhat with surfactant concentration and in the official test method the cloud point is determined by heating a 1% aqueous solution to above clouding and then monitoring the transition from turbid to clear solution on slow cooling of the sample. For surfactants with long polyoxyethylene chains the cloud point may exceed 100°C. For such surfactants determinations are often made in electrolyte

solutions since most salts lower the cloud point. Clouding of non-ionic surfactants is discussed in detail in Chapter 4.

Ethoxylated triglycerides, e.g. castor oil ethoxylates, have an established position on the market and are often regarded as 'semi-natural' surfactants. In recent years there has been a growing interest in fatty acid methyl ester ethoxylates, made from the methyl ester by ethoxylation using a special type of catalyst, e.g. hydrotalcite, a magnesium–aluminium hydroxycarbonate. The methyl ester ethoxylate has the advantage over alcohol ethoxylate in being much more soluble in aqueous solution. Surfactants with high and rapid water solubility, while still having proper surface activity, are needed in various types of surfactant concentrates:

$$R-COOCH_3 + CH_2\underset{O}{-}CH_2 \longrightarrow R-\overset{O}{\underset{||}{C}}-O(CH_2CH_2O)_n-CH_3$$

Alcohol ethoxylates with the terminal hydroxyl group replaced by a methyl or ethyl ether group constitute a category of niche products. Such 'end-capped' non-ionics are made by O-alkylation of the ethoxylate with alkyl chloride or dialkyl sulfate or by hydrogenation of the corresponding acetal. Compared with normal alcohol ethoxylates, the end-capped products are more stable against strong alkali and against oxidation. They are also characterized by unusually low foaming.

Cationics

The vast majority of cationic surfactants are based on the nitrogen atom carrying the cationic charge. Both amine and quaternary ammonium-based products are common. The amines only function as a surfactant in the protonated state; therefore, they cannot be used as high pH. Quaternary ammonium compounds, 'quats', on the other hand, are not pH sensitive. Non-quaternary cationics are also much more sensitive to polyvalent anions. As discussed previously, ethoxylated amines (see Figure 1.7) possess properties characteristic of both cationics and non-ionics. The longer the polyoxyethylene chain, the more non-ionic the character of this surfactant type.

Figure 1.10 shows the structures of typical cationic surfactants. The ester 'quat' represents a new, environmentally friendly type which to a large extent has replaced dialkyl 'quats' as textile softening agents.

The main synthesis procedure for non-ester quaternary ammonium surfactants is the nitrile route. A fatty acid is reacted with ammonia at high temperature to yield the corresponding nitrile, a reaction that proceeds via an intermediate amide. The nitrile is subsequently hydrogenated to primary amine using a cobalt or nickel catalyst:
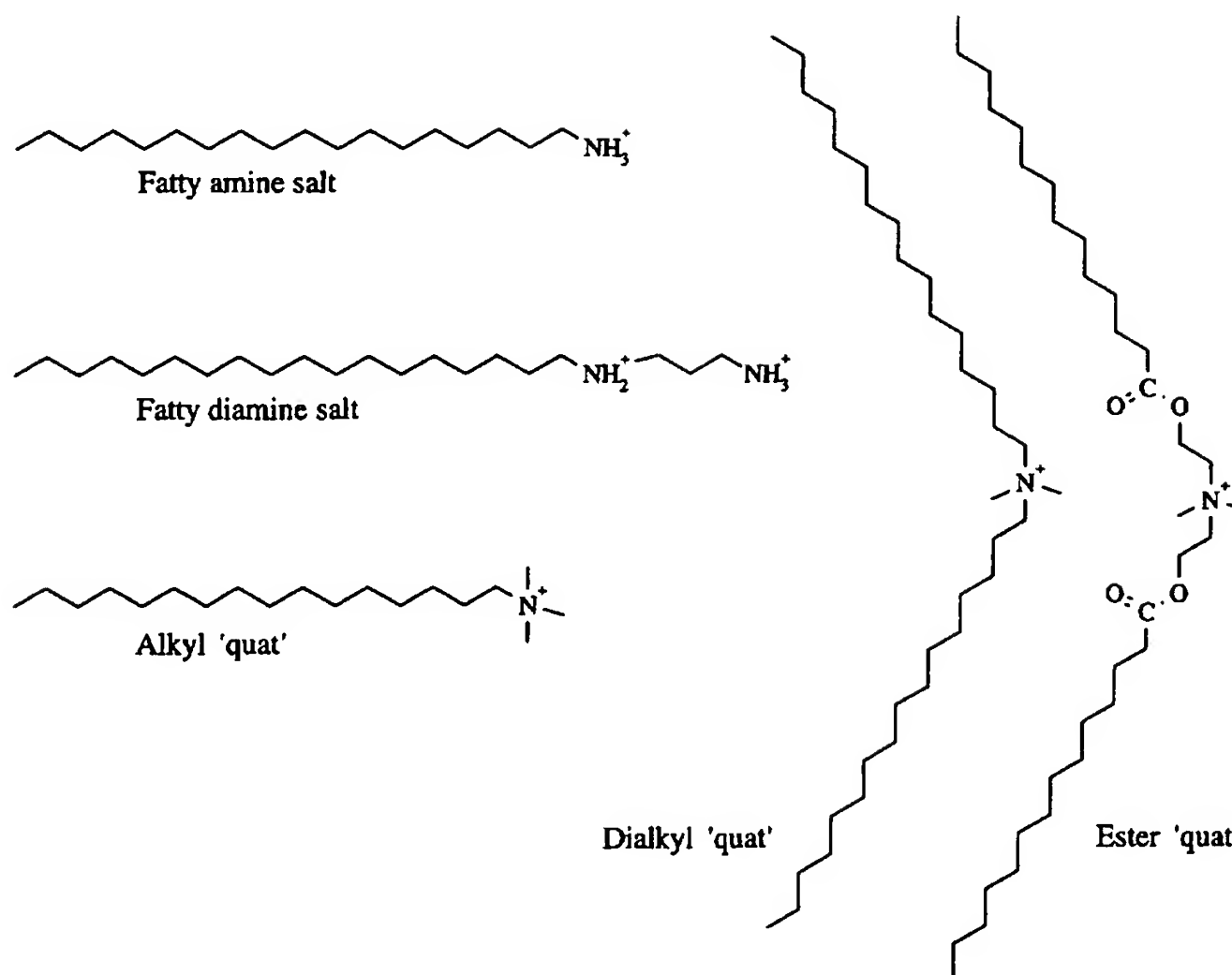
$$R-COOH + NH_3 \xrightarrow{-H_2O} R-C{\equiv}N \xrightarrow{H_2} R-CH_2NH_2$$
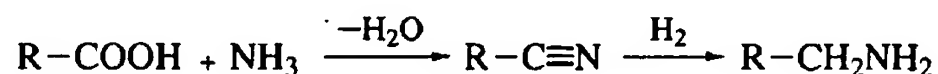
**Figure 1.10** Structures of representative cationic surfactants

Secondary amines can be produced either directly from the nitrile or in a two-stage reaction from the primary amine. In the one-stage route, which is believed to proceed via an intermediate imine, ammonia is continuously removed from the reaction in order to promote secondary amine formation:

$$R-C \equiv N + R-CH_2NH_2 + 2H_2 \longrightarrow (R-CH_2)_2NH + NH_3$$
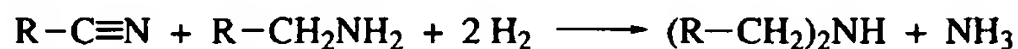
Primary amines can be converted to long-chain 1,3-diamines by cyanoethylation:

$$R-CH_2NH_2 + CH_2{=}CHCN \longrightarrow R-CH_2NH(CH_2)_2CN \xrightarrow{H_2} R-CH_2NH(CH_2)_3NH_2$$

Primary or secondary long-chain alkyl amines can be methylated to tertiary amines, e.g. by reaction with formaldehyde under reducing conditions:

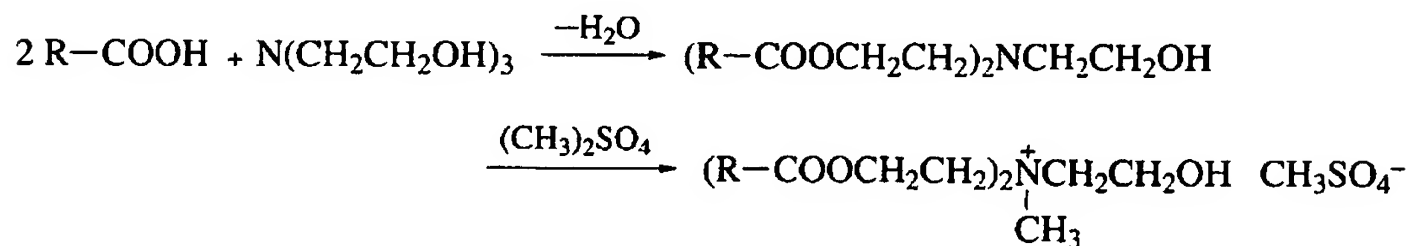$$(R-CH_2)_2NH + HCHO + H_2 \longrightarrow (R-CH_2)_2NCH_3$$
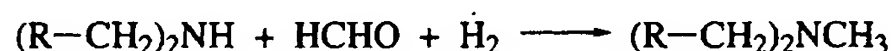
Ethylene oxide can also be used as an alkylating agent to convert primary or secondary amines to tertiary amines with the general structures $R-CH_2N(CH_2CH_2OH)_2$ and $(R-CH_2)_2NCH_2CH_2OH$.

Quarternary ammonium compounds are usually prepared from the tertiary amine by reaction with a suitable alkylating agent, such as methyl chloride, methyl bromide or dimethyl sulfate, the choice of reagent determining the surfactant counterion:

$$(R-CH_2)_2NCH_3 + CH_3Cl \longrightarrow (R-CH_2)_2N^+(CH_3)_2 \; Cl^-$$
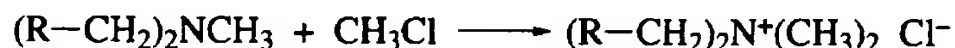
Ester-containing quarternary ammonium surfactants, 'ester quats' are prepared by esterifying a fatty acid (or a fatty acid derivative) with an amino alcohol followed by N-alkylation as above. The process is illustrated for triethanol amine as the amine alcohol and dimethyl sulfate as the methylating agent:

$$2\,R-COOH + N(CH_2CH_2OH)_3 \xrightarrow{\;-H_2O\;} (R-COOCH_2CH_2)_2NCH_2CH_2OH$$

$$\xrightarrow{\;(CH_3)_2SO_4\;} (R-COOCH_2CH_2)_2\overset{+}{\underset{|}{N}}CH_2CH_2OH \; CH_3SO_4^-$$
$$CH_3$$

Nitrogen-based compounds constitute the vast majority of cationic surfactants. However, phosphonium, sulfonium and sulfoxonium surfactants also exist. The first two are made by treatment of trialkyl phosphine or dialkyl sulfide, respectively, with alkyl chloride, as is shown for phosphonium surfactant synthesis:

$$R_3P + R'X \longrightarrow R_3P^+-R' \; X^-$$
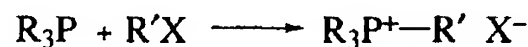
Sulfoxonium surfactants are prepared by hydrogen peroxide oxidation of the sulfonium salt. The industrial use of non-nitrogen cationic surfactants is small since only rarely do they give performance advantages over their less expensive nitrogen counterparts. Surface active phosphonium surfactants carrying one long-chain alkyl and three methyl group have found use as biocides.

The majority of surfaces, metals, minerals, plastics, fibres, cell membranes, etc., are negatively charged. The prime uses of cationics relate to their tendency to adsorb at these surfaces. In doing so they impart special characteristics to the surface. Some examples are given in Table 1.5, while important facts about cationic surfactants are given in Table 1.6.

Zwitterionics

Zwitterionic surfactants contain two charged groups of different sign. Whereas the positive charge is almost invariably ammonium, the source of negative charge may

Table 1.5 Applications of cationic surfactants related to their absorption at surfaces

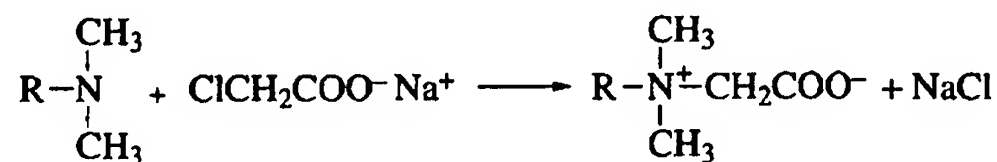| Surface	Application
Steel	Anticorrosion agent
Mineral ores	Flotation collector
Inorganic pigments	Dispersant
Plastics	Antistatic agent
Fibres	Antistatic agent, fabric softener
Hair	Conditioner
Fertilizers	Anticaking agent
Bacterial cell walls	Bactericide

Table 1.6 Important facts about cationic surfactants

1. They are the third largest surfactant class.
2. They are generally not compatible with anionics (although there are important exceptions).
3. Hydrolytically stable cationics show higher aquatic toxicity than most other classes of surfactants.
4. They adsorb strongly to most surfaces and their main uses are related to *in situ* surface modification.

vary, although carboxylate is by far the most common. Zwitterionics are often referred to as 'amphoterics', but as was pointed out on p. 8, the terms are not identical. An amphoteric surfactant is one that changes from net cationic via zwitterionics to net anionic on going from low to high pH. Neither the acid nor the base site is permanently charged, i.e. the compound is only zwitterionic over a certain pH range.
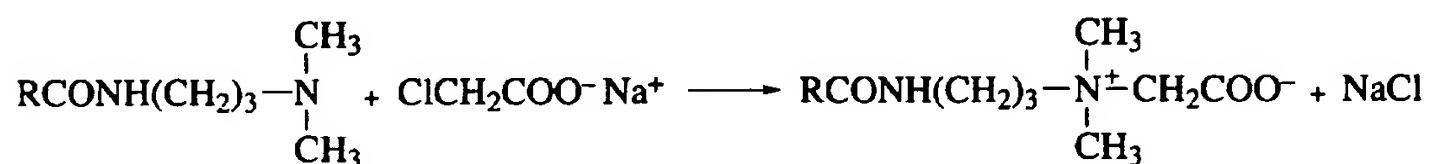
The change in charge with pH of the truly amphoteric surfactants naturally affects properties such as foaming, wetting, detergency, etc. These will all depend strongly on solution pH. At the isoelectric point the physicochemical behaviour often resembles that of non-ionic surfactants. Below and above the isoelectric point there is a gradual shift towards the cationic and anionic character, respectively. Surfactants based on sulfate of sulfonate to give a negative charge remain zwitterionic down to very low pH values due to the very low pK_a values of monoalkyl sulfuric acid and alkyl sulfonic acid, respectively.

Common types of zwitterionic surfactants are N-alkyl derivatives of simple amino acids, such as glycine (NH_2CH_2COOH), betaine (($CH_3)_2NCH_2COOH$) and amino propionic acid ($NH_2CH_2CH_2COOH$). They are usually not prepared from the amino acid, however, but by reacting a long-chain amine with sodium chloroacetate or a derivative of acrylic acid, giving structures with one and two carbons,
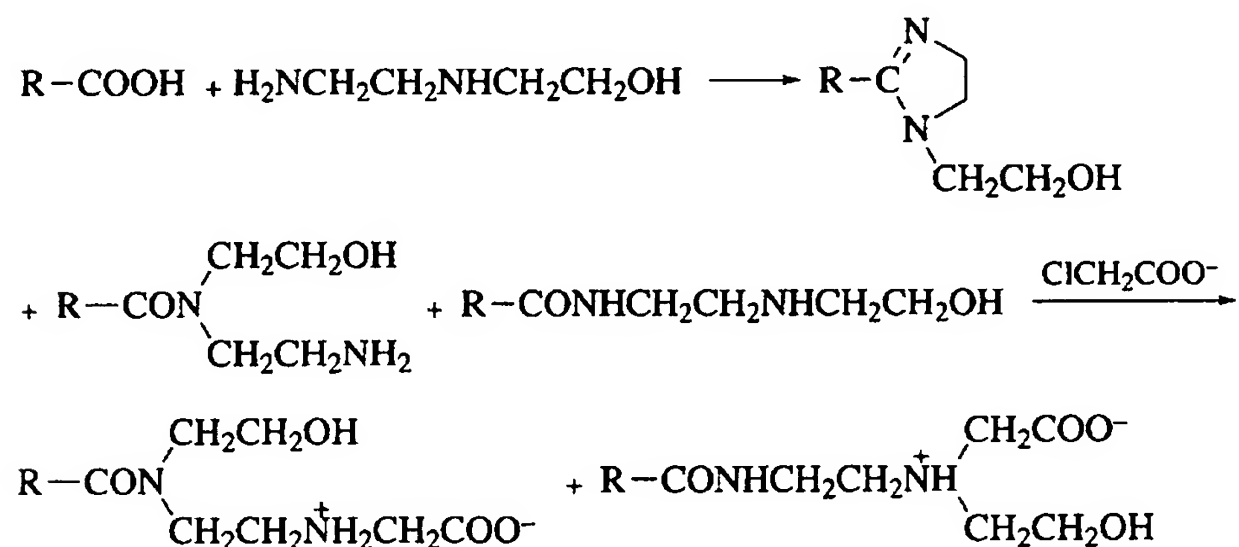
respectively, between the nitrogen and the carboxylate group. As an example, a typical betaine surfactant is prepared by reacting an alkyldimethyl amine with sodium monochloroacetate:

$$
\begin{array}{ccc}
& CH_3 & & CH_3 \\
& | & & | \\
R-N & + ClCH_2COO^-Na^+ \longrightarrow & R-N^{\pm}CH_2COO^- + NaCl \\
& | & & | \\
& CH_3 & & CH_3
\end{array}
$$

Amidobetaines are synthesized analogously from an amidoamine:

$$
\begin{array}{ccc}
& CH_3 & & CH_3 \\
& | & & | \\
RCONH(CH_2)_3-N & + ClCH_2COO^-Na^+ \longrightarrow & RCONH(CH_2)_3-N^{\pm}CH_2COO^- + NaCl \\
& | & & | \\
& CH_3 & & CH_3
\end{array}
$$

Another common type of zwitterionic surfactant, usually referred to as an imidazoline, is synthesized by reaction of a fatty acid with aminoethylethanolamine followed by treatment with chloroacetate. The nomenclature for this surfactant type is a bit confused; it was believed that the products contained an imidazoline ring, but later investigations have shown that the five-membered ring is cleaved during the second synthesis step. A typical reaction sequence is

$$
R-COOH + H_2NCH_2CH_2NHCH_2CH_2OH \longrightarrow R-C
$$

(imidazoline ring structure with N, N-CH₂CH₂OH)

$$
+ R-CON\begin{array}{l} CH_2CH_2OH \\ CH_2CH_2NH_2 \end{array} + R-CONHCH_2CH_2NHCH_2CH_2OH \xrightarrow{ClCH_2COO^-}
$$

$$
R-CON\begin{array}{l} CH_2CH_2OH \\ CH_2CH_2\overset{+}{N}H_2CH_2COO^- \end{array} + R-CONHCH_2CH_2\overset{+}{N}H\begin{array}{l} CH_2COO^- \\ CH_2CH_2OH \end{array}
$$

Zwitterionics as a group are characterized by having excellent dermatological properties. They also exhibit low eye irritation and are frequently used in shampoos and other cosmetic products. Since they possess no net charge, zwitterionics, similar to non-ionics, function well in high electrolyte formulations. A traditional use of the products has been in alkaline cleaners. Figure 1.11 shows examples of typical zwitterionics and Table 1.7 summarizes general information about the surfactant class. As mentioned previously, amine oxide surfactants, or more correctly N-oxides of tertiary amines, are sometimes categorized as zwitterionics, sometimes as non-ionics and sometimes as cationics. They have a formal charge
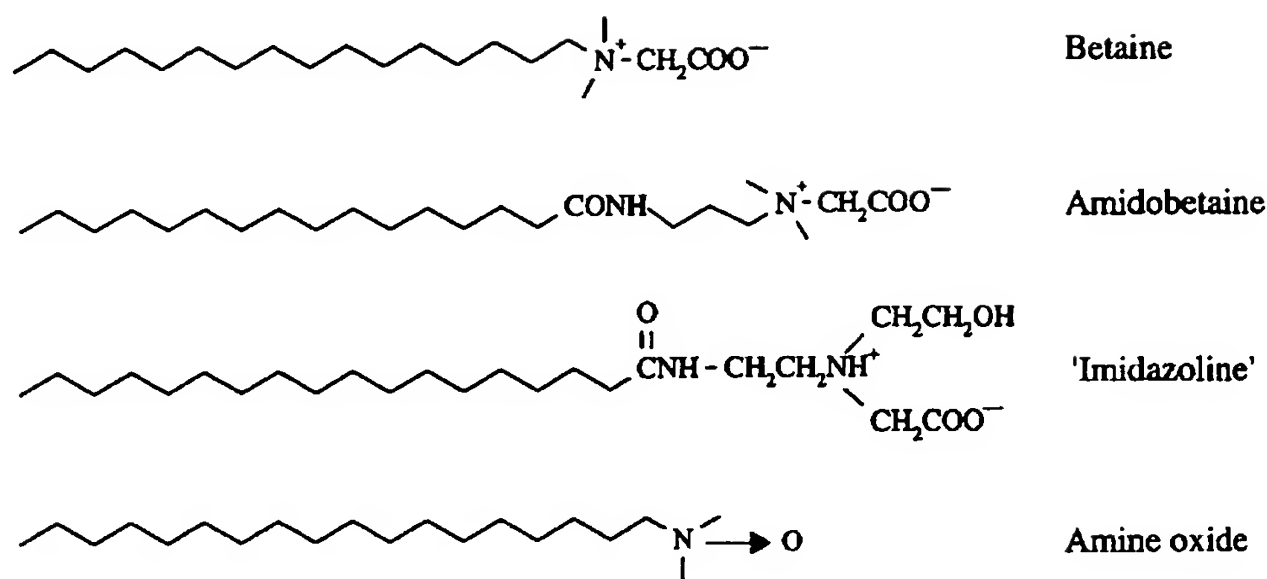
Figure 1.11 Structures of representative zwitterionic surfactants

Table 1.7 Important facts about zwitterionic surfactants

1. They are the smallest surfactant class (partly due to high price).
2. They are compatible with all other classes of surfactants.
3. They are not sensitive to hard water.
4. They are generally stable in acids and bases. Particularly the betains retain their surfactant properties in strong alkali.
5. Most types show very low eye and skin irritation. They are therefore well suited for use in shampoos and other personal care products.

separation on the nitrogen and oxygen atoms. They basically behave as non-electrolytes, but at low pH or in the presence of anionic surfactant they will pick up a proton to form the cationic conjugate acid. A 1 : 1 salt will form between the anionic surfactant and the protonated amine oxide and this salt is very surface active. Amine oxides are prepared by hydrogen peroxide oxidation of the corresponding tertiary amine.

The Ecological Impact of Surfactants is of Growing Importance

Although concern about the ecological impact of surfactants has been enshrined in legislation for more than 20 years, it is only recently that the issue has become a major factor in all formulation work involving surfactants. Most of the surfactants used in households and in industry go into the sewers. The rate of biodegradation in the sewage plant will determine the volume of surfactant that reaches the environment. Rate of biodegradation in combination with the degree of aquatic toxicity will determine the environmental impact. The OECD has issued guidelines and directives regarding:

Aquatic toxicity
Biodegradability
Bioaccumulation

Aquatic Toxicity

Aquatic toxicity may be measured on fish, daphnia or algae. Toxicity is given as LC_{50} (for fish) or EC_{50} (for daphnia or algae; EC stands for effective concentration). Values below 1 mg/l after 96 h testing on fish and algae and 48 h on daphnia are considered toxic. Environment-friendly surfactants should preferably be above 10 mg/l.

Biodegradability

Biodegradation is a process carried out by bacteria in nature. By a series of enzymatic reactions, a surfactant molecule is ultimately converted into carbon dioxide, water and oxides of the other elements. If a product does not undergo natural biodegradation then it is stable and persists in the environment. For surfactants the rate of biodegradation varies from 1–2 h for fatty acids, via 1–2 days for linear alkylbenzene sulfonates to months for branched alkylbenzene sulfonates.

In all testing of biodegradation it is important to realize that the rate of degradation depends on factors such as concentration, pH and temperature. The temperature effect is particularly important. The rate with which chemicals are broken down in sewage plants may vary as much as a factor of 5 between summer and winter in Northern Europe.

Two criteria are of importance with respect to testing for biodegradation: primary degradation and ultimate degradation. Primary degradation of surface active agents relates to the loss of surfactants properties. For instance, an ester surfactant may rapidly break down into alcohol and acid, neither of which is very surface active. This type of test is of interest for specific purposes, e.g. to be able to predict whether or not a product persists in giving foams on rivers.

More important from an ecological point of view is the test for ultimate biodegradation. A plethora of test methods exists for so-called ready biodegradability. In most of these, such as the popular modified Sturm test (OECD test 301 B for ultimate biodegradation), conversion into carbon dioxide is measured as a function of time. With most surfactants there is an induction period followed by a steep rise of the curve and then an abrupt levelling off. A typical test result together with the criteria that must be fulfilled to pass the test is given in Figure 1.12.

Bioaccumulation

Hydrophobic organic compounds are persistent in nature since all biodegradation requires some kind of aqueous environment. Bioaccumulation can be measured
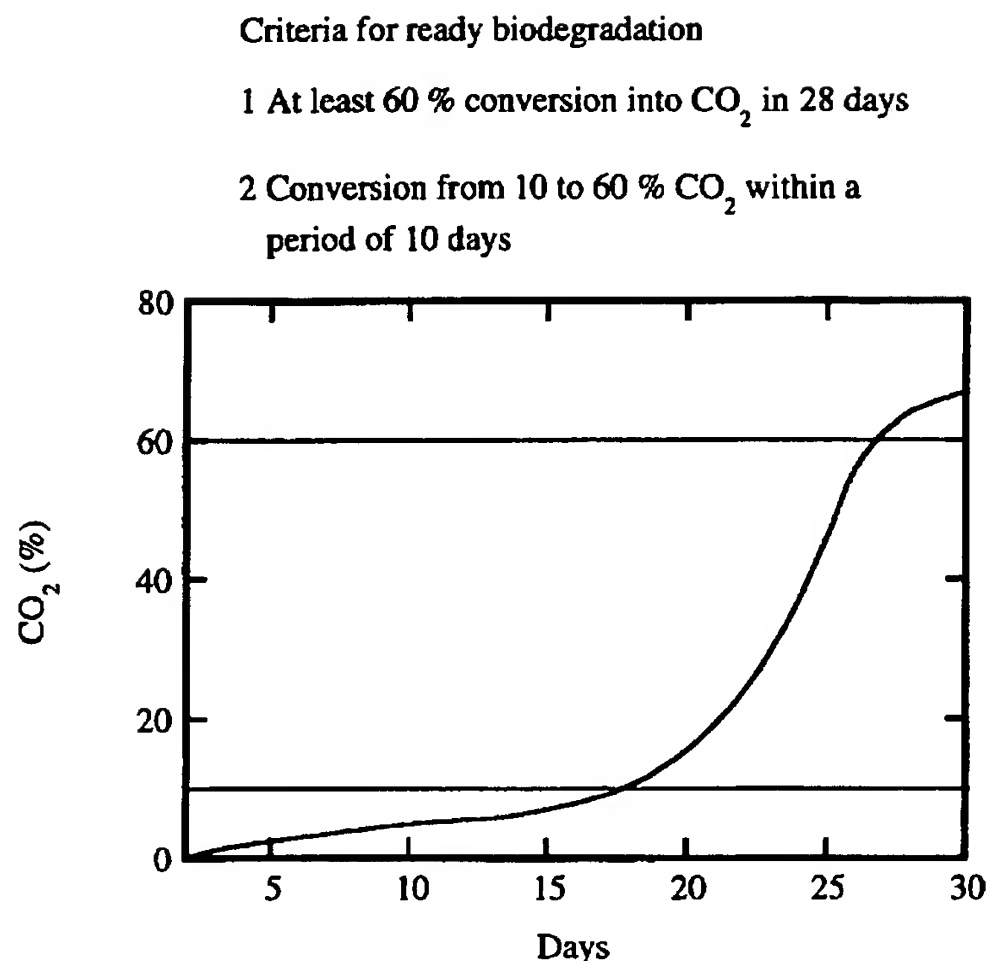
Criteria for ready biodegradation

1 At least 60 % conversion into CO_2 in 28 days

2 Conversion from 10 to 60 % CO_2 within a
period of 10 days

Figure 1.12 Criteria needed to pass the test for ready biodegradability and a typical example of a degradation curve. Note the long induction period before degradation takes off

directly in fish but is more often calculated from a model experiment. Partitioning of the compound between two phases, octanol and water, is measured and the logarithm of the value obtained, log P, is used. (This is a common procedure for assigning hydrophobicity value to organic substances and tables of log P values are available in the literature). A surfactant is considered to bioaccumulate if

$$\log P_{oct/w} > 3$$

The vast majority of surfactants have log P values below 3. Bioaccumulation, therefore, is not considered a crucial issue.

Labelling

In the OECD guidelines for labelling of surfactants, values of aquatic toxicity and ready biodegradation are taken into account. Figure 1.13 illustrates the procedure. Many of the commonly used surfactants today are borderline cases. There is a clear trend to replace these by compounds positioned 'upwards and right' in the diagram.

Tests for aquatic toxicity, ready biodegradation and bioaccumulation by no means give the complete picture of the environmental impact of a surfactant. A
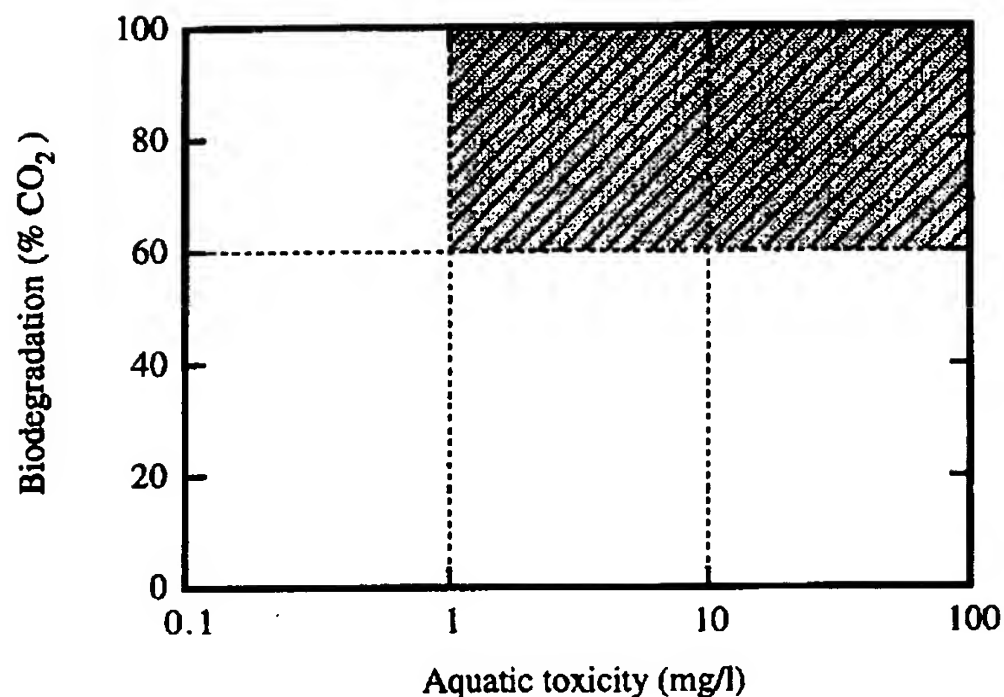
Figure 1.13 Environmental ranking of surfactants is based on the values of ready biodegradation and aquatic toxicity. The shaded areas of the diagram are 'approved areas'

number of other relevant parameters are listed in Table 1.8. In addition, the formulated end-product often contains mixtures of surfactants or a blend of surfactant and polymer. Since it is well-known that the physicochemical behaviour of a surfactant may be very different in such mixtures than alone in solution, it is reasonable to believe that the biological effect may also be different. In order to obtain the full pictures, ecological tests should be done on each individual end-product.

Some Important Development Trends

All major types of surfactants, alkylbenzene sulfonates, alkyl sulfates, alcohol ethoxylates, etc., have been around for decades. Their routes of preparation have

Table 1.8 Relevant factors besides aquatic toxicity, ready biodegradability and bioaccumulation for assessment of surfactant ecotoxicity

1. Anaerobic biodegradation (alkylbenzene sulfonates, alkylphenol ethoxylates and EO–PO block copolymers are examples of surfactants with very slow anaerobic biodegradation)
2. Chronic toxicity
3. Effect on function of sewage plants
4. Toxicity in the production of surfactants
5. Life cycle aspects
6. Technical effect, i.e. the more effective the surfactant, the smaller amount is needed; therefore, biotoxicity per effect unit is the relevant measure (this is particularly relevant for the formulated end-product)

been carefully optimized and their physicochemical behaviour is relatively well understood. Besides the constant challenge of finding ways to minimize the manufacturing cost for existing surfactants, the market pull for 'greener' products has been the overriding driving force for surfactants development in later years. There are also routes of development that have been pursued for technical rather than environmental reasons. In the following a few development trends within the surfactant field will be discussed.

Polyol Surfactants

As mentioned before, the polar head group of non-ionics may consist of either polyether or polyhydroxyl. The polyether chains are normally polyoxyethylene obtained by polymerization of ethylene oxide. Polyhydroxyl (polyol) may be simple sugars, such as glucose or sucrose, other cyclic polyols, such as sorbitan, or acyclic compounds, such as polyglycerols (which may be regarded as a hybrid between polyhydroxyl and polyether). Due to their ease of manufacture, the polyether type of non-ionic is by far the most dominating one. Polyol-based surfactants have been regarded as speciality surfactants. However, they posses several interesting features, some of which are listed in Table 1.9. Taken together, the technical and commercial potential of these surfactants is large enough to induce considerable research and development in search of new surfactant types, improved methods for synthesizing known surfactants and new applications for known surfactants.

Figure 1.14 shows structures of three polyol surfactants of considerable current interest. They are all rapidly biodegradable and show low aquatic toxicity. They differ in their chemical stability. Alkyl glucosides are very stable to alkali and labile to acid. Sugar esters are labile to alkali and fairly stable to acid. Alkyl glucamides, or N-alkanoyl-N-methylglucamines, are stable to alkali and relatively stable to acid. A characteristic features of them all is their tolerance to high electrolyte concentrations. Whereas sugar esters and glucamides contain a defined polar head group, alkyl glucosides have a slightly polymerized sugar chain as the

Table 1.9 Characteristics of polyol surfactants

1. Aerobic and anaerobic biodegradation is fast.
2. Aquatic toxicity is low.
3. Hydroxyl groups are strongly lipophobic. At the same time surfactants with long enough hydrocarbon chains are strongly hydrophobic. Polyol surfactants therefore have a high tendency to remain at the oil-water interface.
4. The effect of temperature on solution behaviour is small and opposite to that of ethoxylates. Mixtures of ionic polyol surfactants (larger fraction) and ethoxylates (smaller fraction) can be formulated so that a non-ionic surfactant with phase behaviour unaffected by temperature is obtained.
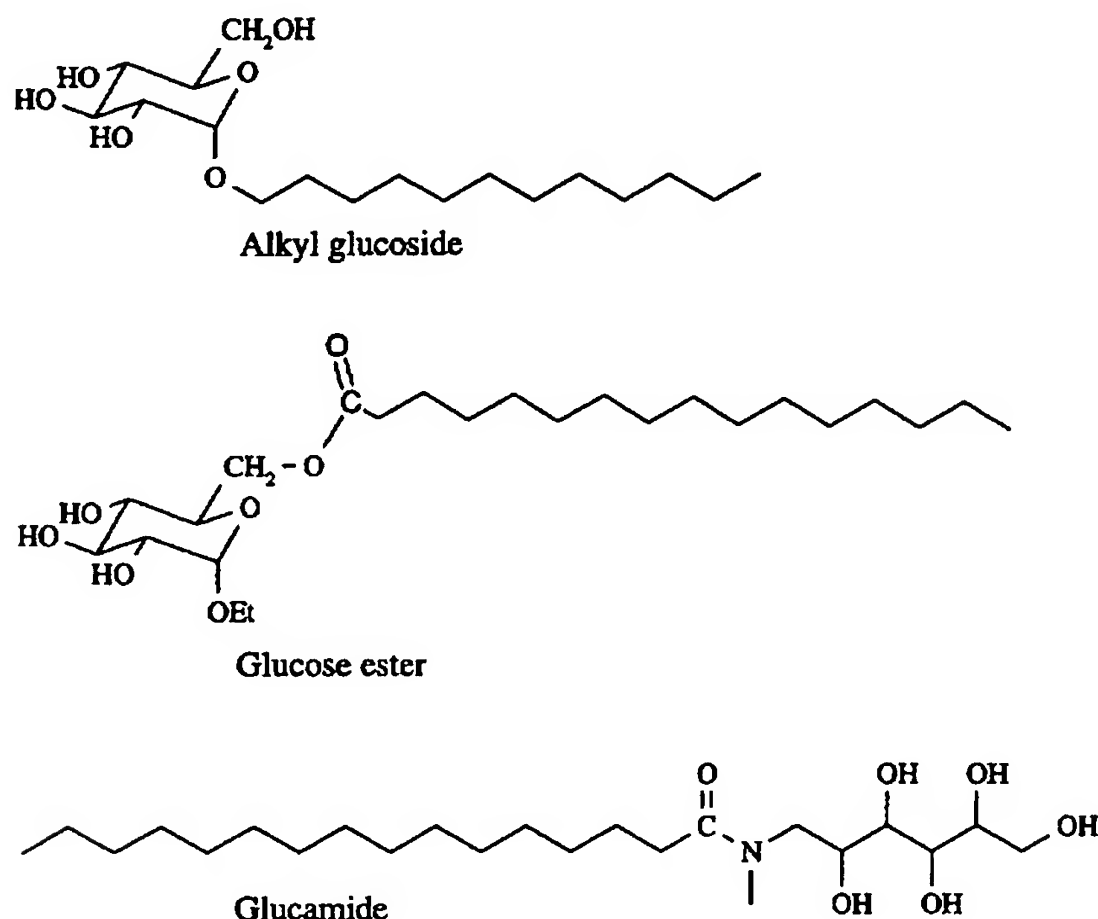
Figure 1.14 Polyol surfactants

hydrophilic group. Normally, the degree of polymerization is between 1 and 2 but surfactants containing longer oligosaccharides can also be prepared.

Alkyl polyglucosides, APGs, are synthesized by direct reaction of glucose with fatty alcohol, using a large excess of alcohol in order to minimize sugar oligomerization. Alternatively, they are made by transacetalization of a short-chain alkyl glucoside, such as ethyl glucoside, with a long-chain alcohol. An acid catalyst is used in both processes. The enzymatic synthesis, using β-glucosidase as catalyst, yields only the β-anomer (but proceeds in very low yield). The corresponding α-anomer can more readily be obtained by β-glucosidase catalysed hydrolysis of the racemate. There are considerable differences in physicochemical properties between the α,β mixture obtained by organic synthesis and the pure enantiomers obtained by the bio-organic route. The β-anomer of n-octyl glucoside has found use as a surfactant in biochemical work.

Sugar esters have traditionally been made by organic synthesis, yielding a complex mixture of esters. Recently, a route based on lipase catalysed esterification of glucose with a fatty acid has been developed. The process yields almost pure 6-monoester.

Alkyl glucamides are prepared by aminolysis of fatty acid ester, usually the methyl ester, using N-methyl glucamine as the nucleophile. Amino esters, obtained if transesterification occurs instead of aminolysis, can be kept at a minimum by proper choice of reaction conditions.

Functional Surfactants

Surfactants having one characteristic chemical property besides that of pronounced surface activity are sometimes referred to as functional surfactants. Examples of functional surfactants are

Polymerizable surfactants
Hydrolysable surfactants

Both types of surfactants are of current interest. Chapter 16 of this book is devoted to polymerizable surfactants. Hydrolysable surfactants will be briefly treated in the following.

Hydrolysable surfactants are surfactants in which a weak bond has been deliberately built in so that controlled breakdown will occur in acid, in alkali, by enzymatic catalysis or by other means. Acetal and ketal bonds are usually employed as acid-labile linkages. Esters are most commonly used to impart alkali sensitivity.

There are several reasons behind the interest for short-lived surfactants. Firstly, surfactants with easily cleavable bonds can be expected to break down rapidly in the environment. Since ecology is an issue of the utmost importance in all uses of surfactants today, the concept of surfactants with weak bonds is intimately linked to the endeavour to find rapidly biodegradable products. Sugar esters and alkyl glucosides are pertinent examples of this, but the concept is probably best illustrated by the ester 'quats' which in a short period of time have taken a major share of the market for conditioners and softeners from the dialkyl 'quats' (see Figure 1.10). Such surfactants can be degraded either by chemical hydrolysis or by a lipase catalysed reaction.

A second incentive for the development of cleavable surfactants is to avoid surfactant-related complications such as foaming or formation of unwanted, stable emulsions. Cleavable surfactants present the potential for elimination of some of these problems. If the weak bond is present between the polar and the non-polar part of the molecule, cleavage will lead to one water-soluble product and one water-insoluble product. Both moieties can usually be removed by standard work-up procedures. This approach has been of particular interest for surfactants used in preparative organic chemistry and in various biochemical applications.

A third use of surfactants with limited stability is to have the cleavage product impart a new function. For instance, a surfactant used in personal care formulations may decompose on application to form products beneficial to the skin. Figure 1.15 illustrates another concept where a surfactant with good detergency properties breaks down under alkaline conditions to a hydrophobic fatty alcohol. Such a surfactant is of interest for combining cleaning and hydrophobization, e.g. when washing tents, rain clothes, etc. By controlling the pH of the formulation, the textiles will be washed and subsequently hydrophobized in a one-step process.

Figure 1.16 illustrates an elegant concept of a surfactant bactericide which breaks down into harmless products, fatty alcohol and betaine. The intact product contains
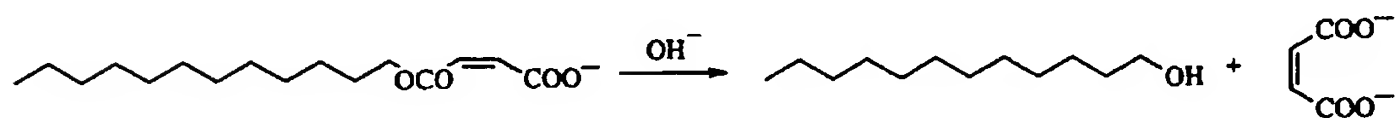
Figure 1.15 Alkaline hydrolysis of an anionic surfactant, a salt of maleic acid half-ester, into a hydrophobic fatty alcohol and water-soluble maleate
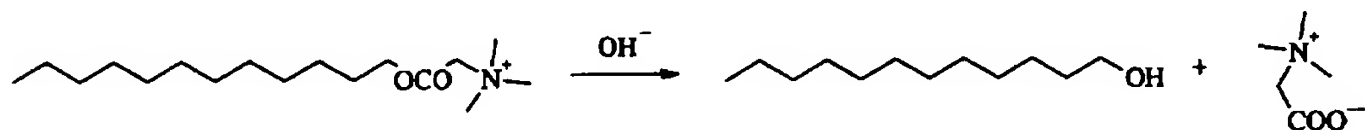

Figure 1.16 Alkaline hydrolysis of a cationic surfactant with biocidal properties into fatty alcohol and betaine

an ester bond with a positive charge adjacent to the carbonyl group. Due to the electron-withdrawing effect of the cationic group, such an ester bond is extremely labile to alkali and correspondingly stable to acid. Small variations of pH, therefore, will have a large effect on the rate of hydrolysis. Such products are of interest in applications where a persistent action of a bactericide is unwanted, e.g. for disinfection in the food and dairy industries.

Light-sensitive surfactants, e.g. compounds containing a diazosulfonate head group, constitute a new interesting type of cleavable surfactant. Such surfactant can be used as emulsifiers in emulsion polymerization. The use of a photolabile emulsifier opens the possibility of controlling the latex coagulation process simply by exposing the dispersion to UV irradiation. The ionic head group of the surfactant will be split off by photolysis, leading to aggregation of the latex particles. Such latexes could be of interest for coatings applications.

Polymeric Surfactants

Polymeric surfactants, or surface active polymers, is an area that is currently attracting much interest. Chapter 10 is devoted to this topic.

Surfactants That Give Extreme Surface Tension Reduction

The vast majority of surfactants have the hydrophobic part of the molecule made up of a hydrocarbon chain, either aliphatic or alkylaryl. With a suitable choice of polar head group the minimum surface tension that can be achieved with such surfactants is in the order of 26–28 mN/m. Such surface activity is sufficient for most uses of surface active agents. However, there are some applications where a lower surface tension of aqueous solutions is required. Spreading of aqueous foams on top of burning oil and spreading of water-based formulations on surfaces of polyolefins are two relevant examples.

Two types of speciality surfactants are used to achieve extreme reduction of surface tension: silicone surfactants and fluorinated surfactants. The former type is

based on polydimethylsiloxane as the non-polar group; the latter contains fluorocarbon or a combination of fluorocarbon and hydrocarbon as the hydrophobic tail. Silicone surfactants are high molecular weight compounds and are treated in Chapter 10. Fluorinated surfactants are briefly introduced below.

Fluorinated surfactants have the general structure

$$CF_3—(CF_2)_n—X$$

or

$$CF_3—(CF_2)_n—(CH_2)_m—X$$

where X can be any polar group, charged or uncharged. The fluorocarbon chain is usually rather short, n typically being 5-9. Fluorinated carboxylates are common. Due to the inductive effect exerted by the electronegative fluorine atoms, these compounds are strong acids and hence are not sensitive to low pH or hard water. There are also perfluorinated block copolymers, analogous to EO-PO block copolymers, on the market.

Fluorinated surfactants are used for various applications where wetting and spreading of aqueous solutions are difficult. Another use of fluorinated surfactants is to render surfaces, e.g. paper or textiles, both hydrophobic and lipophobic. Fluorinated surfactants, like silicone surfactants but unlike hydrocarbon-based surfactants, are also surface active in organic solvents and are therefore used as surfactants in paints and other non-aqueous formulations. The main disadvantage with fluorinated surfactants, besides high price, is their poor biodegradability.

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